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Editorial

Inspection and Palpation of Pulsations on the Front of the Chest

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For many years physicians depended on their eyes and ears to unravel the mysteries of the body. Through necessity some physicians with a keen sense of curiosity learned to examine the surface of the chest and to make rather remarkable deductions about the status of the heart and lungs. The teachings of these physicians have been handed down, though modified, ever since. During the last two decades new and wonderful recording equipment has revived the interest in careful physical examination, since scrutiny of the records has shown that there is more to be found than was suspected. We must become curious again—this time, influenced by the records obtained from the recording equipment—and try to extract all the information possible from simple bedside examinations, using our eyes, hands, and ears. This should be done before going on to the more time-consuming, expensive, and occasionally painful types of examination. The latter types of examinations are frequently needed before a complete appraisal of the problem can be made; but it is wrong, in our opinion, to utilize the more complicated types of examination before the physical examination is complete. For example, it is distressing to hear a student state that he must know the results of cardiac catheterization before giving an opinion in a case of suspected congenital heart disease, and to discover that he has overlooked many diagnostic clues when performing the physical examination.

It is pleasing to observe that careful physical examination is receiving attention again. Accordingly, it seems fitting to emphasize the information that can be obtained by looking at and feeling the front of the chest.[1]

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AREAS OF THE CHEST TO BE EXAMINED

As with everything else in the field of medicine, one finds only what one looks for. Therefore, it is necessary to specifically examine five areas of the front of the chest.

Area 1. The Sternoclavicular Joints.—When one sees or feels a pulsation in the right or left sternoclavicular joint, one should consider an abnormality of the ascending aorta or the arch of the aorta.

Area 2. The Pulmonary Artery Area.—The second and third intercostal spaces adjacent to the sternum are considered to be the region of the pulmonary artery. Pulsation in this area can be the result of pulmonary hypertension or increased pulmonary arterial flow.

Area 3. The Anterior Precordium.—The lower portion of the sternum and the adjacent precordium on the left is called the anterior precordium. This area may pulsate abnormally when there is right ventricular hypertrophy or myocardial infarction.

Area 4. The Apical Area.—The apical impulse is located in this area. This impulse may become abnormal when there is left ventricular hypertrophy or myocardial infarction.

Area 5. The Epigastric Area.—Pulsations in the epigastric area are due either to right ventricular hypertrophy in patients with emphysema, aortic pulsations, or liver pulsations.

METHOD OF EXAMINATION

The following suggestions dealing with the method of examination are very simple but, nevertheless, important. (1) Inspect and feel the anterior portion of the chest while the patient is lying down in a relaxed position. (2) A "warm-up" period is needed for inspection and palpation. Everyone is familiar with the delay encountered when trying to feel the dorsalis pedis artery. A similar delay occurs when one examines the anterior surface of the chest. Several minutes of looking and feeling may be required before one sees or feels an abnormal pulsation. (3) The apical impulse may seem to be small when it is first located. After searching the surrounding area, one may note that the impulse extends over a larger area than was first found. At times, one or two ribs may overlie a large area of pulsation, causing the examiner to misinterpret the size of the impulse. (4) A flashlight is useful in identifying areas of pulsation. The rays should shine tangentially from the right across the anterior and left lateral surfaces of the chest in order to see pulsations with maximum efficiency. (5) The most important factor is to become sufficiently interested in the examination to specifically search for pulsations.

Examination of Area 1. (*The Sternoclavicular Joints*).—Pulsations of the right or left sternoclavicular joint usually indicate that something is wrong with the aorta. The right or left clavicular joint may pulsate when there is an aneurysm of the aorta of sufficient size to lie adjacent to the sternoclavicular area. Logue and Sikes[2] pointed out that a dissecting aneurysm of the aorta will occasionally cause pulsation of the right or left sternoclavicular joint. Accordingly, it is wise to search for such an important diagnostic clue in patients with chest

pain. A right-sided aortic arch is usually higher than the normal left-sided arch and can cause pulsation of the right sternoclavicular joint.

Examination of Area 2. (*The Pulmonary Artery Area.*)—A prominent pulsation in the pulmonary area usually means that the pulmonary artery is dilated from either an elevated pressure or an increased pulmonary blood flow, or a combination of both. The pulmonary artery is likely to be dilated when there is mitral stenosis, interatrial septal defect, interventricular septal defect, primary pulmonary arteriolar disease, or patent ductus arteriosus. Slight pulsation of this particular area may occur also in healthy, young, normal subjects.

Examination of Area 3. (*The Anterior Precordium*).—The anterior precordium is considered to be the lower portion of the sternum and the adjacent precordium on the left. The portions of the heart that lie beneath this region and cause pulsation of the area are the right ventricle and interventricular septum. The following four conditions should be considered when examining the anterior precordium.

1. Normally very little pulsation can be seen or felt in the area of the anterior precordium in the quiet, normal person.

2. When there is an increased cardiac output such as occurs in anxiety, anemia, fever, thyrotoxicosis, peripheral arteriovenous fistula, etc., a pulsation can be detected in the anterior precordial region when the heart is normal, as well as when it is enlarged. This type of pulsation is not localized and not sustained. The pulsation can be felt only during a brief portion of the cardiac cycle.

3. When there is right ventricular hypertrophy, the lower portion of the sternum and the area of the chest to the left of the sternum may actually "lift" the palpating hand. This type of pulsation is said to be sustained. The cause of this pulsation is not completely understood. It is believed that the right ventricle swings anteriorly and to the right under normal conditions. When the right ventricle is thick and enlarged, this type of movement becomes exaggerated to such a degree that the anterior precordium pulsates abnormally. When there is right ventricular hypertrophy due to congenital heart disease, the anterior precordium, including the sternum, may actually bulge anteriorly, while acquired right ventricular hypertrophy is less likely to cause such an anatomic deformity of the bony cage. Pulsation of the anterior precordium is not likely to occur in patients with advanced pulmonary emphysema, even when there is right ventricular hypertrophy, since the anterior portion of the chest is separated from the anterior portion of the heart.

4. A prominent pulsation can be detected occasionally in the anterior precordial region following myocardial infarction. The exact cause of this pulsation is not known. It is likely, however, that the pulsation represents a "physiologic aneurysm." Two facts should be kept in mind—one is that the septum is an anterior structure, and the other is that many infarcts involve the septum. It seems reasonable to expect such a pulsation after anterior myocardial infarction only. However, no studies are available which allow one to state with certainty that it never occurs after inferior or posterior infarction. It is possible that even a posterior septal infarction might weaken the septum in such

a manner as to allow an anterior pulsation. The abnormal pulsations that follow myocardial infarction are now being studied and will be the subject of a later report.

Examination of Area 4. (The Apical Area).—The exact cause of apical impulse in the normal subject is not known. Harrison[1] and others have suggested that the recoil of the right ventricle, plus a physiologic normal aneurysm of the left ventricle, may result in the pulsation. The latter—the physiologic normal aneurysm—is thought to occur because the base of the left ventricle is thicker than the apex of the left ventricle. Accordingly, when cardiac contraction occurs, the apex of the heart balloons out to some degree. There is much to learn about the apical impulse, but the following four things must not be forgotten.

1. The normal subject may or may not have a visible or palpable apical impulse. When an apical impulse is found, it is necessary to determine the size, the location, and the duration of the pulsation. Normally, the apical impulse is small and localized, affecting an area smaller in size than a half-dollar piece, is located near the left mid-clavicular line, and has a brief duration. The ability to judge the duration of a pulsation requires practice, but it is one of the most important parts of the examination. The apical impulse tends to remain small and merely taps the finger even when the normal heart is displaced laterally.

2. When there is left ventricular hypertrophy, the apical impulse may cover an area larger in size than a half-dollar piece but may be inside, near, or outside the left mid-clavicular line. The apical impulse tends to be sustained. The physiologic normal aneurysm of the left ventricle becomes exaggerated. *The forceful, sustained lifting of the fingers is the most diagnostic sign of left ventricular hypertrophy.* This clue to left ventricular hypertrophy may be present when the heart size is normal to x-ray examination. We agree with Harrison[1] that percussion is a poor method of examination of the heart and that, at best, it can be termed a crude way to determine heart size. Inspection and palpation of the apical impulse—as well as of other precordial pulsations—are more reliable than percussion and, also, yield additional information. Percussion enables one to determine the location of the borders of cardiac dullness. Inspection and palpation allow one to determine the location, the size, and the duration of the apical impulse—three things to study rather than one.

The impulse that is characteristic of left ventricular hypertrophy is not ordinarily seen when there is right ventricular hypertrophy; however, we have had cases in which the right ventricular impulse was felt laterally and suggested left ventricular hypertrophy. Despite the occasional exception, tight mitral stenosis can usually be excluded when one finds the typical left ventricular hypertrophy type of apical impulse. At times, the combination of right and left ventricular hypertrophy can be suspected by inspection and palpation. We believe that more errors will be made when judging the presence of combined ventricular hypertrophy than when determining pure right or pure left ventricular hypertrophy, although some information may be obtained under such circumstances.

3. Abnormal pulsations in the apical region may be the result of anterior myocardial infarction. Vakil[3] found abnormal pulsations in 5.7 per cent of patients with myocardial infarction and described three types of abnormality:

(a) a single precordial pulsation, 2 to 6 cm. in diameter, internal to and above where the apical impulse should be, (b) a single wide area of pulsation, 6 to 7 cm. in diameter, caused by the fusion of the abnormal pulsation with a palpable apical beat, and (c) two distinct areas of pulsation—"a double impulse"—due to the apical beat and the pulsation from a myocardial infarction. In the majority of cases the abnormal pulsations just listed are transitory, lasting from 4 to 24 days. Occasionally, a true anatomic ventricular aneurysm results from myocardial infarction and the abnormal pulsation may become permanent.

4. A visible and palpable pulsation can be detected at the apex in some patients with a ventricular diastolic gallop (protodiastolic gallop). In fact, the gallop pulsation occasionally can be seen and felt more readily than the gallop sound can be heard. This sound, occurring after the second sound, at the end of the first third of diastole, implies myocardial weakness.

Examination of Area 5. (*The Epigastric Area*).—Pulsations in the epigastric region may be produced by the heart or the aorta. When there is considerable pulmonary emphysema, then the right ventricular pulsations may be felt in the epigastrium. A useful method of examination is to "slide" the fingers under the rib cage in the epigastric region; the right ventricular impulse will strike the end of the fingers, while the pulsations of the abdominal aorta will strike the palmar surface of the fingers.

A WARD STUDY OF FIFTY PATIENTS

The anterior and lateral surfaces of the chest were inspected and palpated for pulsations in 50 patients at the Grady Memorial Hospital. Whether heart disease was present in the majority of patients, and if so, of what type, was not known by us at the time of the examination. Since heart disease is one of the most frequent reasons for admitting patients to Grady Hospital, we expected to find considerable heart disease in the group. The only other requirement for this study was that the patients should have an electrocardiogram and an x-ray of the chest, so that cardiac hypertrophy could be studied by these techniques. This requirement would also weigh the data for more heart disease. Two observers compared their impressions and agreed closely except in two cases. No effort was made to compare the results of percussion with the results of inspection and palpation, for the reason that it soon became obvious that we could not perform an impartial examination using the method of percussion after having performed careful inspection and palpation. We soon learned that percussion was a cruder form of examination and yielded much less information than did inspection and palpation. During the study it was pleasing to note that the interest of the house staff increased in regard to the inspection and palpation of pulsations on the anterior surface of the chest.

The study involved too few patients to draw any statistical information, but the following points were of interest.

An impulse was felt in 44 of 50 patients. Although most cases with left ventricular hypertrophy had the apical impulse located beyond the mid-clavicular line, 2 cases of left ventricular hypertrophy had abnormal apical impulses at or inside the mid-clavicular line. Both of these had left ventricular hypertrophy

with hearts normal in size by x-ray, but with definitely abnormal electrocardiograms. There were 3 patients with apical impulses beyond the mid-clavicular line who did not have evidence of left ventricular hypertrophy by x-ray or electrocardiogram. There was an increased size of the apical impulse in the majority of patients with left ventricular hypertrophy, and there was only one proved case that did not have an increased size. Accordingly, if an apical impulse definitely covers an area larger in size than a half-dollar piece, left ventricular hypertrophy is likely to be present. The apical impulse was sustained in the majority of cases of left ventricular hypertrophy. Since only one proved case of left ventricular hypertrophy did not have a sustained impulse, it is our distinct impression that a sustained impulse is probably the most reliable indication of left ventricular hypertrophy. Left ventricular hypertrophy was diagnosed by inspection and palpation of the precordium in 16 of 50 patients. Eleven of these cases had evidence of left ventricular hypertrophy on the electrocardiogram, 2 had right and left ventricular hypertrophy by x-ray with normal electrocardiograms, and 3 had recent myocardial infarction. In 4 cases the observers were not willing to state that the apical impulse was definitely abnormal or definitely normal. Two of the cases proved to have diseases that would cause combined ventricular hypertrophy.

Five cases were diagnosed as having right ventricular hypertrophy on the basis of inspection and palpation of the precordium. All 5 cases had evidence for right ventricular hypertrophy, and had electrocardiogram or x-ray confirmation of right ventricular hypertrophy. In 2 cases the observers were unwilling to state that the anterior precordial pulsations were definitely abnormal or definitely normal. When studied by electrocardiogram and x-ray, both of these cases proved to have left ventricular hypertrophy due to hypertension. This perhaps emphasizes that the most common cause of right ventricular hypertrophy is left ventricular heart failure.

Six of 10 cases of recent myocardial infarction showed abnormal pulsations on physical examination. Three of these had associated left ventricular hypertrophy.

CONCLUSION

On the basis of our "blind" study of 50 ward patients it is our conclusion that careful inspection and palpation of the anterior chest enables one to diagnose left ventricular hypertrophy and right ventricular hypertrophy in a surprisingly large percentage of patients. Myocardial infarction also causes abnormal precordial pulsations, and these should be looked for more frequently. In efforts to determine the presence of ventricular hypertrophy it is necessary to inspect and palpate the anterior precordium in addition to obtaining an electrocardiogram and a chest x-ray.

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Electrocardiogram and Vectorcardiogram Reconstruction and Its Application to Clinical Diagnosis of Myocardial Infarction

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INTRODUCTION

It is well known that electrocardiographic changes[1-20] in the patient with myocardial infarction are characterized by Q phenomenon associated with RS-T deviation and T deformation in the early stage of the episode, and also by Q phenomenon associated with T deformation in old myocardial infarction. Corresponding changes in the vectorcardiogram have been reported by many authors[21-24]; that is, some specific portion of the QRS loop is directed away from the infarcted area in old myocardial infarction.

The question as to why such changes appear has not yet been definitely answered. In the electrocardiogram the Q phenomenon has been explained according to the concept of an electrical "window."[40] However, this concept is not applicable to the explanation of changes in the vectorcardiogram.

In 1952, Toyoshima and collaborators[25-27] explained the serial changes of the QRS complex during the evolution from fresh to old stages of myocardial infarction by the bipolarity theory of Wilson. Thereafter, they began reconstruction of electrocardiograms and vectorcardiograms.[28,29] They recognized[30,31] that the changes in the electrocardiogram and vectorcardiogram during the progress of myocardial infarction could be explained very well by the bipolarity theory, so far as it is concerned with the QRS complex or QRS loop. They also recognized that the authors' explanations of the serial changes of Q phenomenon during the progress of myocardial infarction from fresh to old were correct.

In the present report, reconstruction of electrocardiograms and vectorcardiograms in cases with myocardial infarction was performed with the aid of the table of solid angle measurements prepared by Toyoshima and associates.[32] The measurements in the table were obtained from a heart model consisting of 5 blocks, as described in the same paper.

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The electrocardiographic and vectorcardiographic changes in myocardial infarctions were previously reported by Toyoshima and collaborators.[30] The aim of the preceding study was different from that of the present one and, to our regret, the spreading process of ventricular activation dealt with in the former report was not elaborate enough to discuss in detail. Electrical potentials due to activation of subendocardial muscles were obtained by presumptive calculations from the electrical potentials due to corresponding subepicardial muscles in proportion to distance and area, because the solid angles subtending each unit area of endocardial surface were not measured in that report. In this report, such defects are corrected.

Up to the present time, the changes of QRS complex in the electrocardiogram have been explained by the change of the solid angle subtended by the activated area. However, no studies with actual measurements of the solid angles have been reported. What will be the features of the electrocardiograms and the vectorcardiograms if they are reconstructed from the values of the solid angle preliminarily measured? The answer to this question is another objective of the present study.

METHOD

Reconstructions were performed using the table[32] of solid angle measurements obtained from the heart model. The solid angles presented in the table are the results of measurements on many small, equal-sized areas on the endocardial, septal, and epicardial surfaces of the heart.

According to the current concept of heart muscle electrophysiology,[33] the muscle cell membranes in resting condition are polarized uniformly throughout the heart, thus making an electric double layer; the heart is electrically noneffective to points outside the cardiac muscles. But, when a part of the ventricle is affected by activation, the muscle cell membranes of that area will be depolarized, and the electric double layer with closed surface will be broken at that region; thus, the heart will become electrically effective to every point of the body. The electrical potential at a given point, caused by depolarization of those muscles, is determined by the degree of the solid angle subtended by the depolarized area at that point.

It is possible, therefore, to obtain a potential change during the QRS interval at a given lead-point by summing up the values of the solid angles subtended by each equal-sized, small area of the ventricular surfaces, which have been preliminarily measured, corresponding to the spread of ventricular activation. In old myocardial infarction, the infarcted region can be treated as electrically silent, and in fresh infarction, as in a polarized state being fully or partially unresponsive.

Six different locations of the infarcted area were included in the present study. The locations (anteroseptal, anterolateral, anteroposterior, lateral, posterolateral, and posterior positions) are illustrated in Fig. 1. These locations are very similar to those in Myers' reports,[10-15] with some minor modifications by the authors. Most of the cases in the present report are treated as old transmural infarctions.

The original processes of the spread of ventricular activation used in this study were the two illustrated in Figs. 2*A* and 2*B*. They produced two different types of electrocardiographic pattern, namely, semivertical and semihorizontal electrical heart positions, as seen in Figs. 3*A* and 3*B*. It is seen that different types of electrical heart position may possibly appear even in a heart with the same anatomic position. The two processes adopted here are considered normal in various points of view.

The values of the potentials at a given point during the interval from the instant when the front of the spreading wave of activation began to contact the infarcted area, to the instant when the wave of activation included the infarcted area completely, were obtained approximatively from the equations in Fig. 4. Various relationships between the spread of activation and the position of the areas of infarction could be classified in 8 cases, such as are illustrated in Fig. 4.

These 8 cases were studied in 4 stages in the following manner: (1) A stage in which the activation that has occurred at a certain region of the subendocardial muscles is affecting the subendocardial muscles adjacent to the infarcted area, but the front has not yet reached any part of the epicardial surface (*1*, Fig. 4). (2) A stage in which the activation has affected all subendocardial muscles surrounding the infarct and has not yet affected any part of the subepicardial muscles (*2*, Fig. 4). Stages 1 and 2 occur early in ventricular activation. (3) A stage in which the activation is affecting the subepicardial muscles after Stage 2 (*3* to *6*, Fig. 4). (4) A stage in which the activation is affecting the subepicardial muscles after Stage 1, and yet activation does not spread to the line which includes the endocardial portion of the infarct entirely within it (*7* and *8*, Fig. 4).

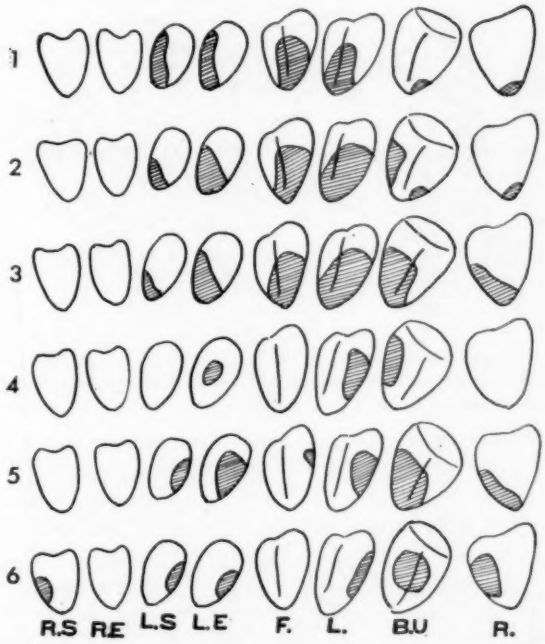

Fig. 1.—The positions of the infarcted areas. From above downward: anteroseptal, anterolateral, anteroposterior, lateral, posterolateral, and posterior infarctions; and from the reader's left to right: right septal, right free endocardial, left septal, left free endocardial, frontal, left lateral, back-caudal, and right lateral views of the ventricles.

In the stage in which the activation front is in contact with the infarcted area during activation spreads through the free ventricular wall from within to without, the solid angle subtended by the surface of the wave front at a given point outside the cardiac muscles cannot be obtained from the tables of the solid angle measurements. Thus, the electrical potential in this stage must be obtained from the solid angle values of the epicardial surface by means of a proportion using the equations shown in *2* of Fig. 4.

In Fig. 4, the dotted areas show the areas which have completed depolarization, the hatched areas indicate infarcted areas, and the heavy dotted lines represent the front of activation. φ is the unknown potential. Ω is the value of solid angle, and the notation Ω_{AC}, for example, designates the solid angle value subtended by the surface within marks A and C at a given lead-point.

When right or left bundle branch was complicated, electrocardiograms and vectorcardiograms were reconstructed on the basis of the propagation processes having been planned appropriately to these blocks.

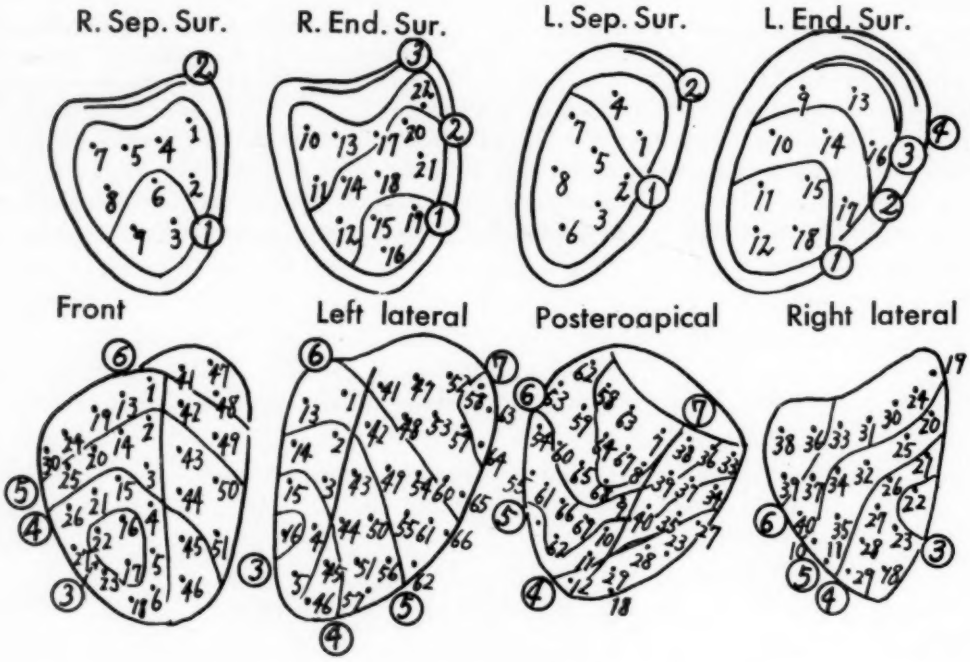

Fig. 2*A*.—A process of the spread of ventricular activation utilized for the reconstruction of normal electrocardiograms of semihorizontal electrical heart position and vectorcardiograms illustrated in Fig. 3*A*.

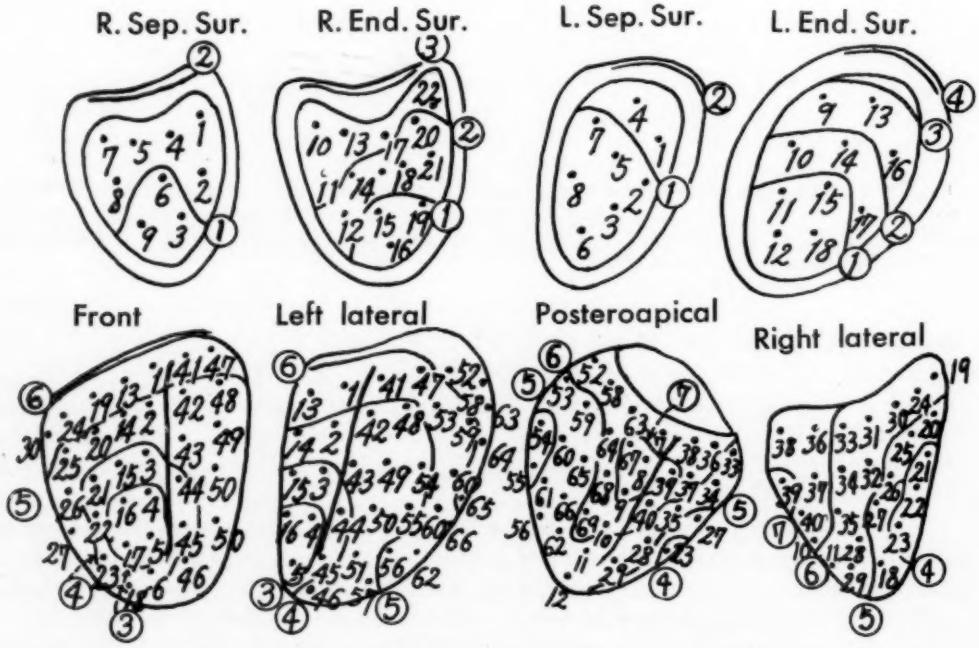

Fig. 2*B*.—A process of the spread of ventricular activation utilized for the reconstruction of normal electrocardiograms of semivertical electrical heart position and vectorcardiograms illustrated in Fig. 3*B*.

RESULTS

When each of the infarctions of 6 different locations occurred independently, the electrocardiograms and the vectorcardiograms changed in ways such as are shown in Figs. 5*A*, 5*B*, 6*A*, and 6*B*. The original patterns of these electrocardiograms and vectorcardiograms were those illustrated in Figs. 3*A* and 3*B*.

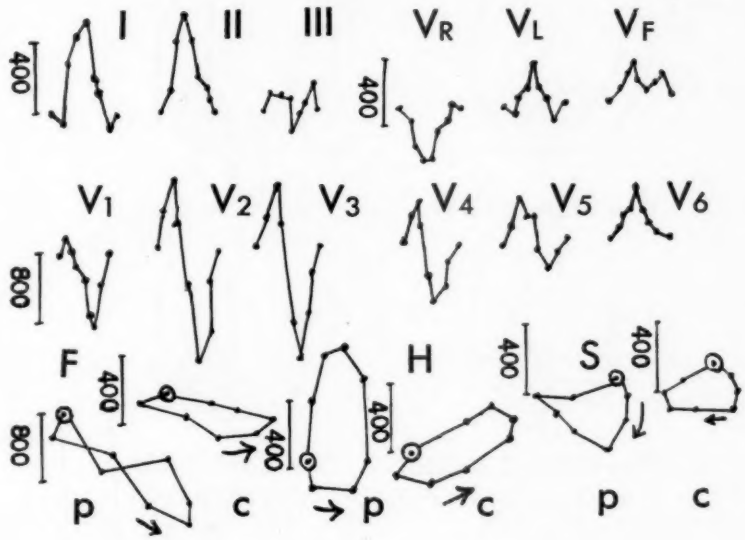

Fig. 3*A*.—The electrocardiograms and the vectorcardiograms reconstructed according to the process illustrated in Fig. 2*A* (a case of semihorizontal electrical heart position).

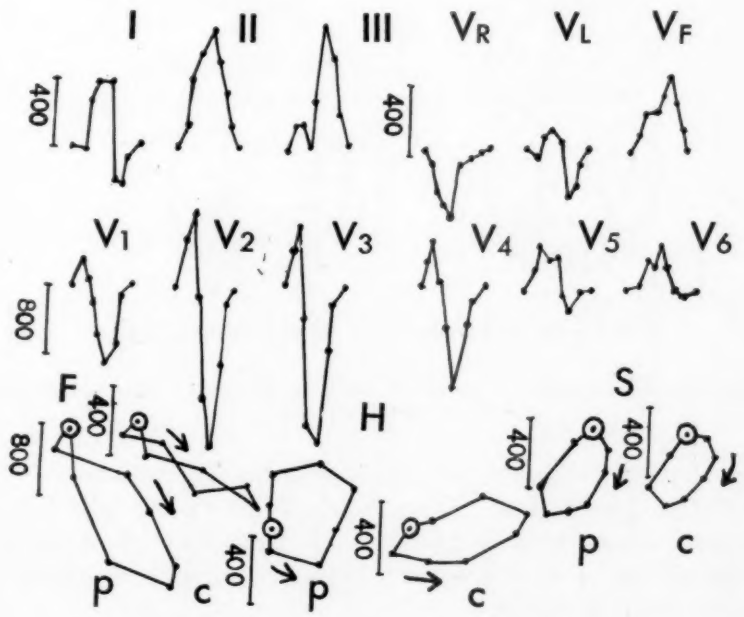

Fig. 3*B*.—The electrocardiograms and the vectorcardiograms reconstructed according to the process illustrated in Fig. 2*B* (a case of semivertical electrical heart position).

The processes of the spread of ventricular activation producing these original electrocardiograms and vectorcardiograms were those shown in Figs. 2*A* and 2*B*, where *A* is the propagation process which gave rise to the electrocardiogram of semihorizontal electrical heart position, and *B* is the propagation process which gave rise to the electrocardiogram of semivertical heart position.

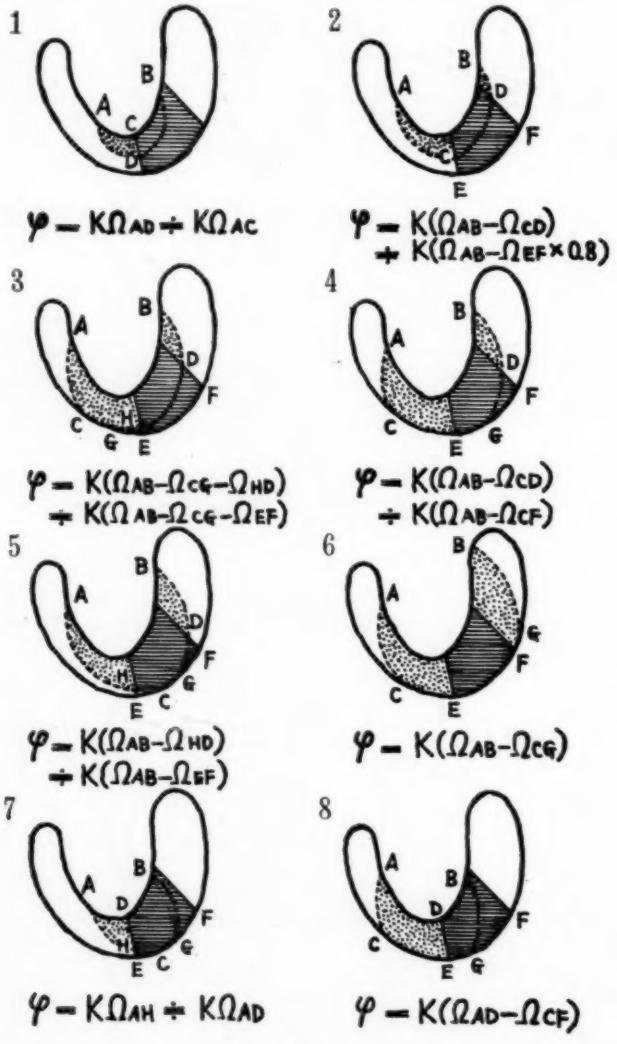

Fig. 4.—Equations for the calculation of potentials when the infarcted area is in various relationships to the spread of activation.

Electrocardiographic Changes in Old Myocardial Infarctions.—

1. *Anteroseptal infarction:* From Leads V_1 to V_5 the initial R waves decreased and the S waves increased; from Leads V_1 to V_3 Q phenomena occurred. No particular difference was observed between the electrocardiograms from propagation processes *A* and *B*.

2. *Anterolateral infarction:* The initial R wave increased in Lead V_1, but decreased in Leads V_2 to V_6, and Q phenomena appeared in Leads V_4 to V_6.

The S wave in Lead V_R decreased and showed a slight tendency for an initial R and/or late R to appear, but in Leads V_4 to V_6 the S waves increased. Again, no particular difference was noted between processes *A* and *B*.

3. *Anteroposterior infarction:* The initial R wave increased in Lead V_1 but decreased in Leads V_3 to V_6, and Q phenomena appeared in Leads V_3 to V_6. In Lead V_R the S wave decreased and initial r and/or late r waves appeared.

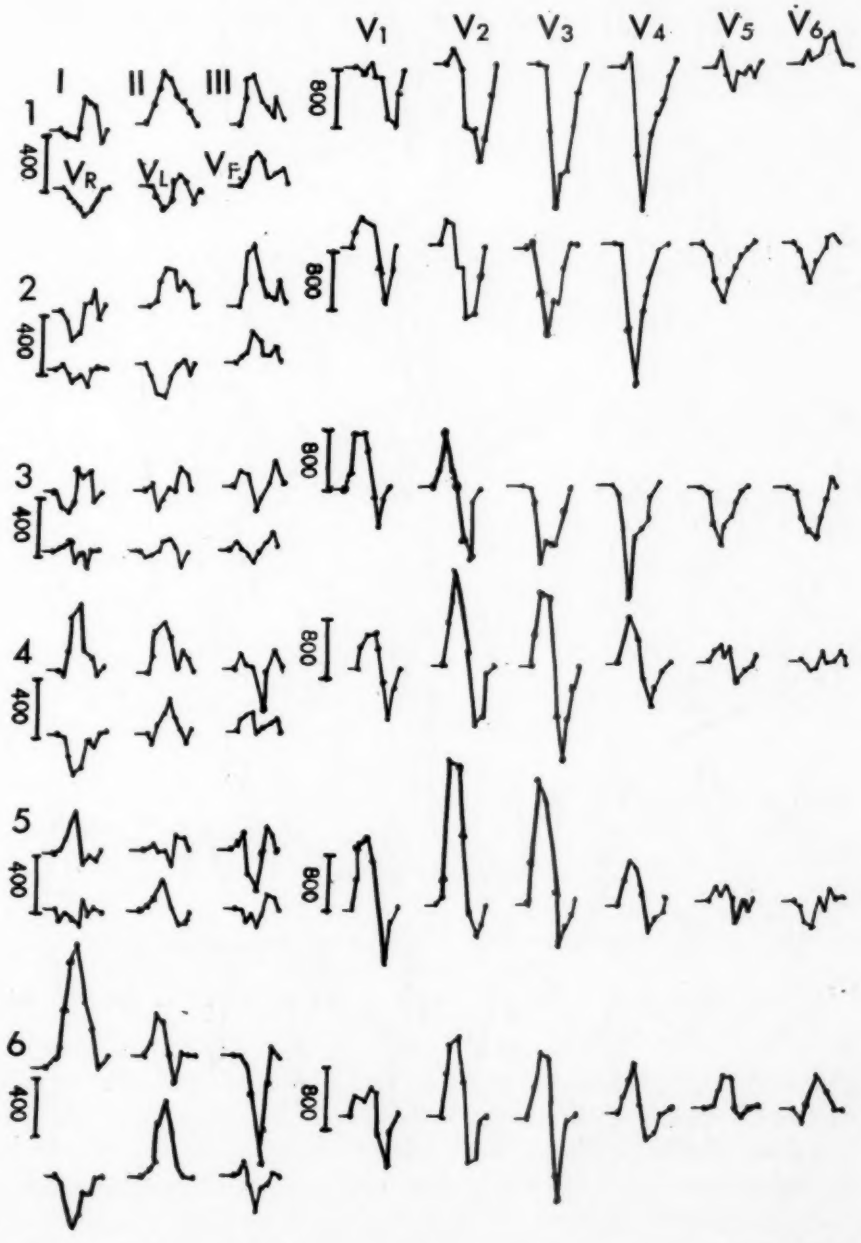

Fig. 5*A*.—The electrocardiographic changes in old myocardial infarctions of six different locations (originated from the process in Fig. 2*A*).

The R wave in Lead V_F decreased and showed a tendency for a Q wave to appear. In general, the amplitude in the limb leads became small in both processes.

4. *Lateral infarction:* The R waves in Leads V_1 to V_3 increased, but those in Leads V_5 and V_6 decreased. A Q wave appeared in Lead V_6. The pattern of

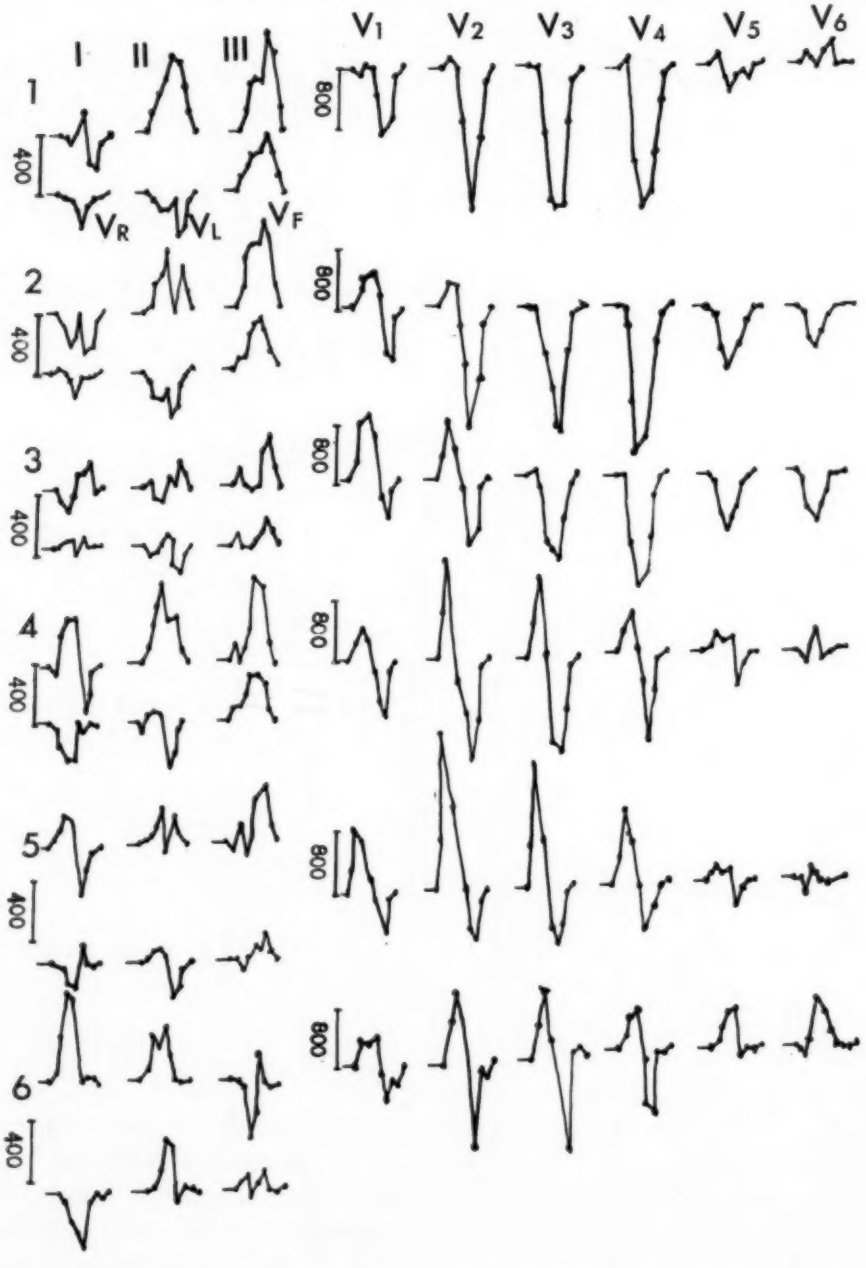

Fig. 5*B*.—The electrocardiographic changes in old myocardial infarctions of six different locations (originated from the process in Fig. 2*B*).

the limb leads in process *A* was much different from that in process *B*. In the case of *A*, it was R_I and S_{III} pattern, but in the case of *B*, QRS was concordant in every lead.

5. *Posterolateral infarction:* In Leads V_1 through V_4, the R waves increased and the S waves decreased. In Lead V_6 a Q wave appeared. The patterns of the limb leads in both cases were also quite different from each other. In process *A* it was R_I and S_{III} pattern, but in the case of *B* it was S_I and R_{III} pattern. In Lead V_F the R wave decreased and a Q wave appeared.

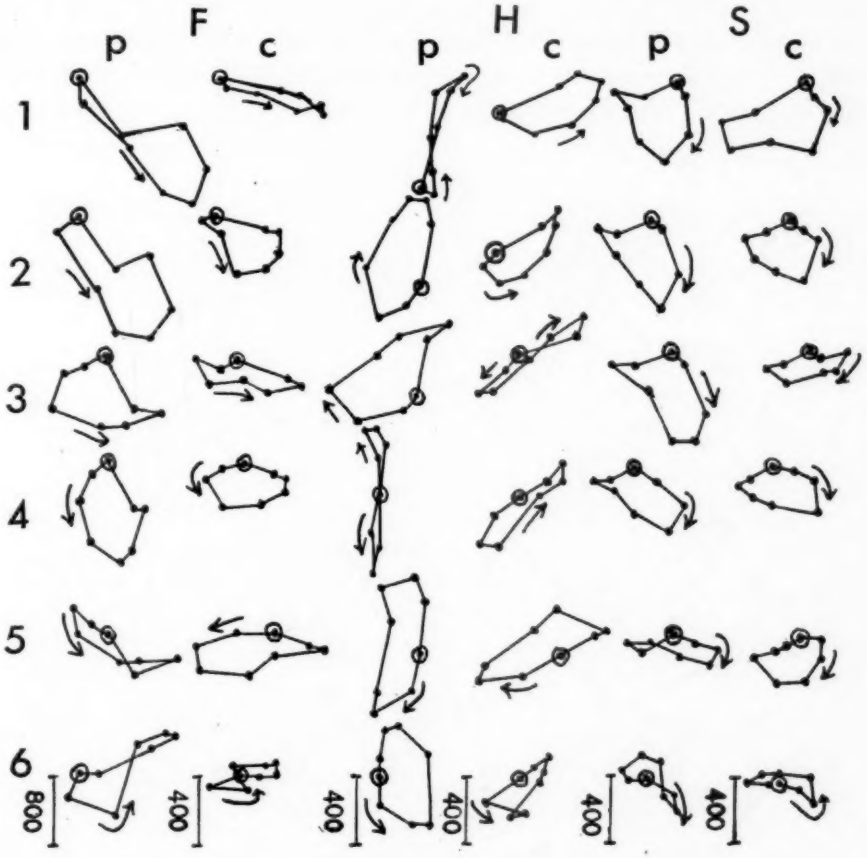

Fig. 6*A*.—The vectorcardiographic changes in old myocardial infarctions of six different locations (the same cases as in Fig. 5*A*).

6. *Posterior infarction:* In Leads V_1 through V_4 the R waves increased and the S waves decreased. In Lead V_6 a Q wave appeared. In Lead V_F the R wave decreased and showed a tendency for a Q or q wave to appear. The pattern of the limb lead was always that of R_I and S_{III} in both processes.

In infarctions of 5 different locations, excepting anterior infarction, the initial R wave in Lead V_1 became larger either with or without development of a late R in Lead V_R. In myocardial infarctions involving the lateral to posterior aspects of the ventricular wall, the initial R waves in Leads V_1 to V_3 or V_4 became larger.

Electrocardiographic Changes in Fresh Infarctions.—In this part of the report the description of the changes is limited to the infarctions in the case of propagation process *A*, because the trend of the changes in the cases of propagation process *B* was nearly the same as that in process *A*. In all fresh myocardial infarctions, in which the cell membranes of muscles in infarcted areas are supposed to be in maximal polarization but unresponsive to the stimuli, the deviation of the RS-T segment was the most impressive of the features, and the Q wave did not appear except in Lead V_1 in anteroseptal infarction (see Fig. 7).

1. *Anteroseptal infarction:* RS-T segments from Leads V_2 through V_6 were elevated and that of Lead V_1 was depressed. Elevation was most impressive in Leads V_3 and/or V_4. The RS-T segment in Lead V_R was depressed and those in Leads V_L and V_F were elevated; consequently, the elevation of the RS-T segments in Leads I and II resulted.

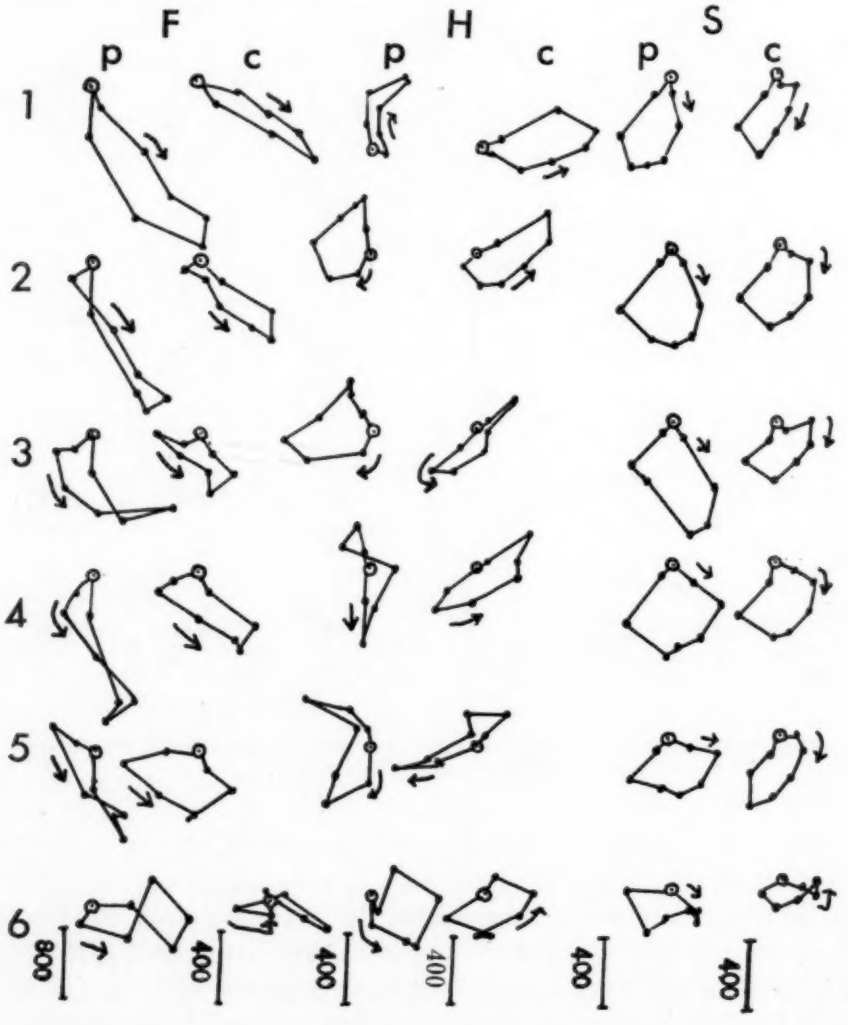

Fig. 6*B*.—The vectorcardiographic changes in old myocardial infarctions of six different locations (the same cases as in Fig. 5*B*).

2. *Anterolateral infarction:* Changes in the electrocardiograms were nearly the same as those in anteroseptal infarction, except for the presence of initial r wave in Lead V_1.

3. *Anteroposterior infarction:* RS-T segments in Leads V_1 and V_2 became depressed and those in Leads V_3 through V_5, elevated. In extremity leads, the RS-T segment in Lead V_R became depressed and that in Lead V_F, elevated; hence the elevation of RS-T segments in 3 standard bipolar leads resulted.

4. *Lateral infarction:* In precordial leads the RS-T segments in Leads V_1 through V_6 became depressed, especially in V_1 to V_3. Changes in RS-T segments in unipolar extremity leads were not so pronounced; hence those in 3 standard bipolar leads were also not remarkable.

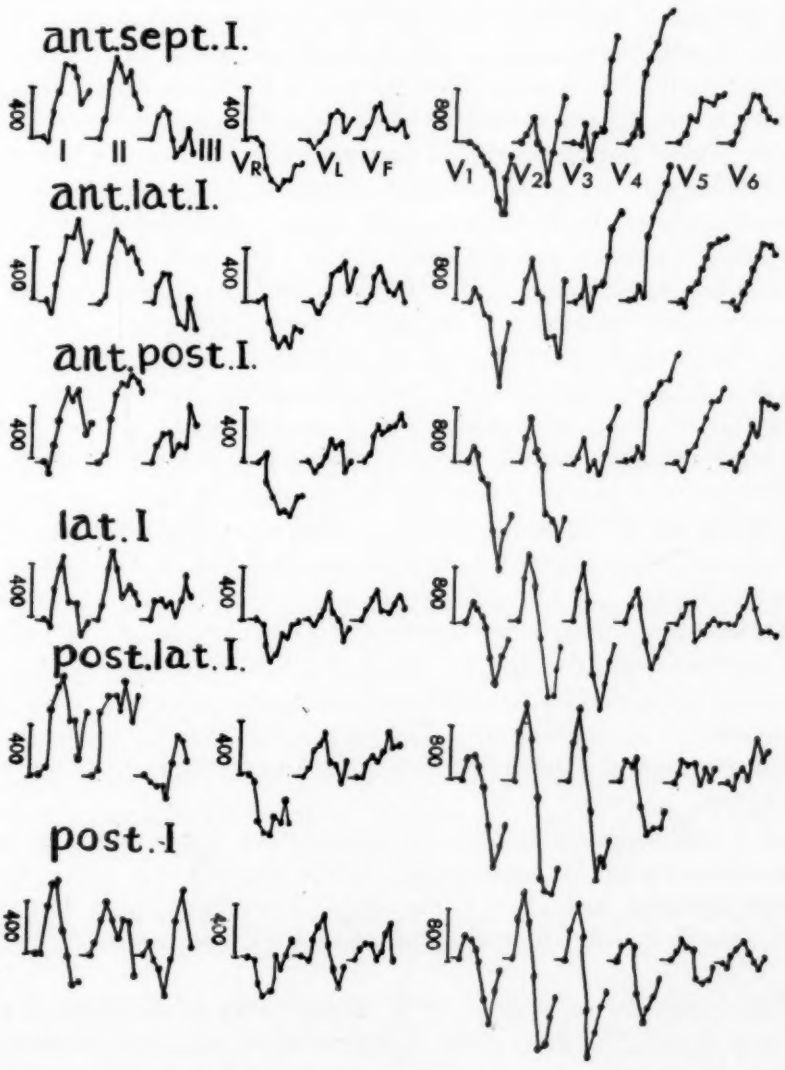

Fig. 7.—The electrocardiographic changes in fresh myocardial infarctions of six different locations. (Originated from the process in Fig. 2*A*. Compare with those in Fig. 5*A*.)

5. *Posterolateral infarctions:* RS-T segments in Leads V_1 through V_4 became depressed and those in Leads V_5 and V_6, elevated. In unipolar extremity leads, the RS-T segment in Lead V_R became depressed and that in Lead V_F elevated, with elevation of RS-T segments in all 3 bipolar leads resulting.

6. *Posterior infarction:* RS-T segments in Leads V_1 through V_5 were depressed and that in Lead V_6 was slightly elevated. In unipolar extremity leads the RS-T segment in Lead V_R was elevated and that in Lead V_F, slightly elevated. In the bipolar extremity leads, therefore, depression of RS-T segments in Leads I and II resulted.

Significant differences in the electrocardiographic findings between fresh and old myocardial infarctions were as follows: In fresh infarction the displacement of the RS-T segment was impressive in every lead, especially in those leads over the infarcted area. Q phenomenon typical of old myocardial infarction did not yet appear in most of the leads. Generally, in fresh infarction the RS-T depression in the precordial lead electrocardiograms was seen in the leads which presented a more prominent R wave than normal in old myocardial infarction, and the elevation of the RS-T segment in fresh infarction was observed in the leads in which the Q phenomenon or distinct reduction of the R wave was seen in old myocardial infarction. In the unipolar extremity leads the tendency of the changes was the same. In most fresh infarctions, except posterior infarction, the RS-T segment in Lead V_R was depressed.

Vectorcardiographic Changes in Old Myocardial Infarctions.—

1. *Anteroseptal infarction:* The initial forces of QRS loop (portion from the first to the fourth stage of the spread of ventricular activation in illustrations) were displaced to the posterior, and the deformation was most pronounced in the horizontal and sagittal planes. The most important characteristics were the lack of the initial deflection which is oriented anteriorly to the right, and, instead, inscription of the QRS loop to the left posterior in the horizontal plane. The direction of the inscription in the horizontal plane was not necessarily counterclockwise, but often clockwise, depending upon the heart position and the extent of infarction.

2. *Anterolateral infarction:* The initial forces to the mid-portion of the QRS loop (portion from the first to the sixth stage of the spread of ventricular activation) were displaced to the right posterior, most intensively in the horizontal plane, especially in the polyogram. The important finding was the existence of the initial inscription of a deflection anteriorly and to the right in the horizontal plane QRS loop.

But this finding is not specific for anterolateral infarction. In infarctions of other positions, except for anteroseptal infarction, the initial deflection pointing toward right anterior was always inscribed. The direction of the inscription was not necessarily counterclockwise, but often clockwise, especially in the polyogram.

3. *Anteroposterior infarction:* The initial forces to the terminal portion of the QRS loop (portion from the first to the seventh stage of the spread of ventricular activation) shifted to the right posterior and somewhat to the superior direction from the original position. In the present example, the direction of

the inscription changed from counterclockwise to clockwise in the horizontal plane in the polyogram, while the QRS loop by the cube system inscribed a figure-of-eight before and after infarction.

4. *Lateral infarction:* The intermediate portion (portion from the second to the fifth stage of the spread of ventricular activation) was displaced mainly to the right of the original position. The deformation was most marked in the horizontal and the sagittal plane projections of the vectorcardiogram. In the sagittal plane, the component inscribed anteriorly became larger than the normal. The direction of the horizontal QRS-loop inscription in the polyogram changed from counterclockwise to a figure-of-eight.

5. *Posterolateral infarction:* The major portion of the QRS loop (portion from the second to the seventh stage of the spread of ventricular activation) was inscribed to the right anterior. The direction of the inscription of the QRS loop in the horizontal plane changed from counterclockwise to clockwise in both methods, and the component inscribed anteriorly in the sagittal plane became larger than the normal.

6. *Posterior infarction:* The major portion of the QRS loop (portion from the second to the seventh stage of the spread of ventricular activation) was displaced to the anterior-superior, and the deformation was most pronounced in the frontal and sagittal planes. The initial forces inscribed anteriorly in the sagittal plane became larger than the normal and occupied a more anterior position than the normal.

Vectorcardiographic Changes in Fresh Infarctions.—The vectorcardiographic changes in fresh infarctions of various positions were typified by displacement of the RS-T junction directed toward the infarcted area. In association with the displacement of the RS-T junction, the terminal portion was also displaced toward the infarcted area (see Fig. 8). Tracings in Fig. 8 are an example of vectorcardiograms in fresh myocardial infarctions of 6 different positions. They were originated from the propagation process *A* in Fig. 2. In both cases of propagation process, *A* and *B*, the vectorcardiographic changes were nearly the same.

In fresh infarction most of the QRS loops did not return to their isopotential points, and the displacement of the RS-T junction toward the infarcted areas resulted. The terminal portion was displaced toward the infarcted area, in contrast to the displacement of the initial portion directed away from the infarcted area in old myocardial infarction.

The period in which the displacement of inscription occurs differs between fresh and old myocardial infarctions. In old myocardial infarction it is from the instant in which the front of the activation wave is provided with a contact with the infarcted area to the instant in which the front of the activation wave gives up its contact with the infarcted area; whereas the period in fresh infarction is from the former instant to the end of the QRS loop.

Electrocardiographic and Vectorcardiographic Changes in Right Bundle Branch Block Complicated by Left Ventricular Myocardial Infarction.—

Electrocardiographic changes: When myocardial infarction was complicated by right bundle branch block, a Q wave was also observed in the leads over the

infarcted area, that is, even though right bundle branch block was complicated, appearance of a Q wave in the heart with myocardial infarction was not disturbed by the complication of right bundle branch block.

Tracings in Fig. 10 are examples of electrocardiographic changes in myocardial infarctions complicated by right bundle branch block. The pattern of the propagation process of ventricular activation in this case of right bundle branch block is illustrated in Fig. 9, and the original features of the electrocardiograms and vectorcardiograms resulting from this pattern of ventricular activation are illustrated at the tops of Figs. 10 and 11. In this pattern of propagation process, the process in the right ventricle was planned to be activated earlier in the posterior than in the anterior wall.

Extremity lead electrocardiograms displayed the usual type of right bundle branch block. Leads V_1 and V_2 showed a tall R wave but no Q and S waves. In the left side of the standard precordial leads, however, the R waves were significantly small and the S waves were markedly large. The features of these electrocardiograms are somewhat abnormal in the magnitude of the R waves in

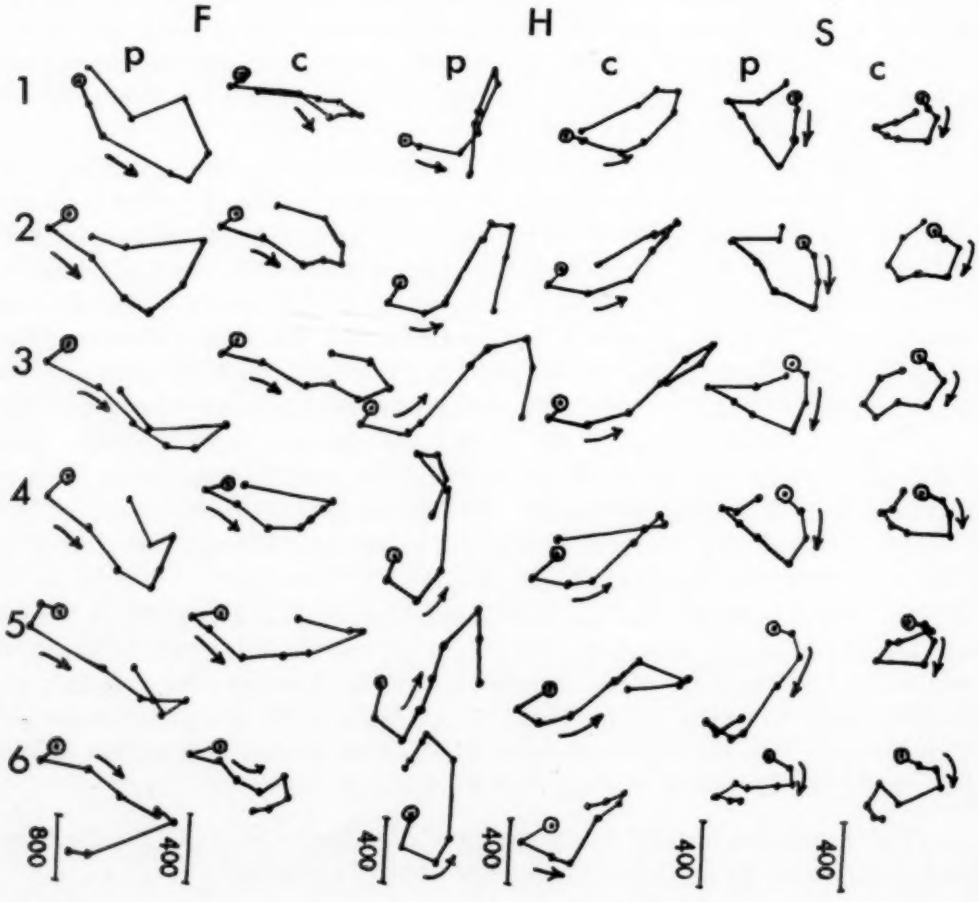

Fig. 8.—The vectorcardiographic changes in fresh myocardial infarctions of six different locations. (Originated from the process in Fig. 2*B*. Compare with those in Fig. 6*B*.)

the left side of precordial leads. This is probably due to inappropriateness of planning the propagation process, but they display significantly the characteristics of electrocardiographic changes in right bundle branch block.

Changes of precordial lead electrocardiograms after the complication of myocardial infarction with right bundle branch block were nearly the same in both cases of propagation pattern of ventricular activation. However, the pattern of extremity lead electrocardiograms varied with the pattern of propagation process and with the location of the infarcted area. Every kind of pattern, the usual and unusual type of Wilson block and the rare type of bundle branch block, was observed in extremity lead electrocardiograms. (Details will be reported elsewhere.)

In general, the electrocardiographic pattern of the rare type of bundle branch block was observed in myocardial infarction of anterior aspect. The pattern of the unusual type of Wilson block was observable only in myocardial infarction of posterior aspect, especially in the case in which the posterior wall of the right ventricle was activated earlier than the anterior wall.

Vectorcardiographic changes: Tracings in Fig. 11 are examples of vectorcardiographic changes corresponding respectively to the electrocardiographic changes shown in Fig. 10.

The characteristics of the vectorcardiographic changes in right bundle branch block, in which the mid- to terminal portion is inscribed anteriorly to the right inferior, were not modified by complication of left ventricular myocardial infarction of any position. The terminal portion especially was scarcely displaced from its original position even after the complication of myocardial infarction

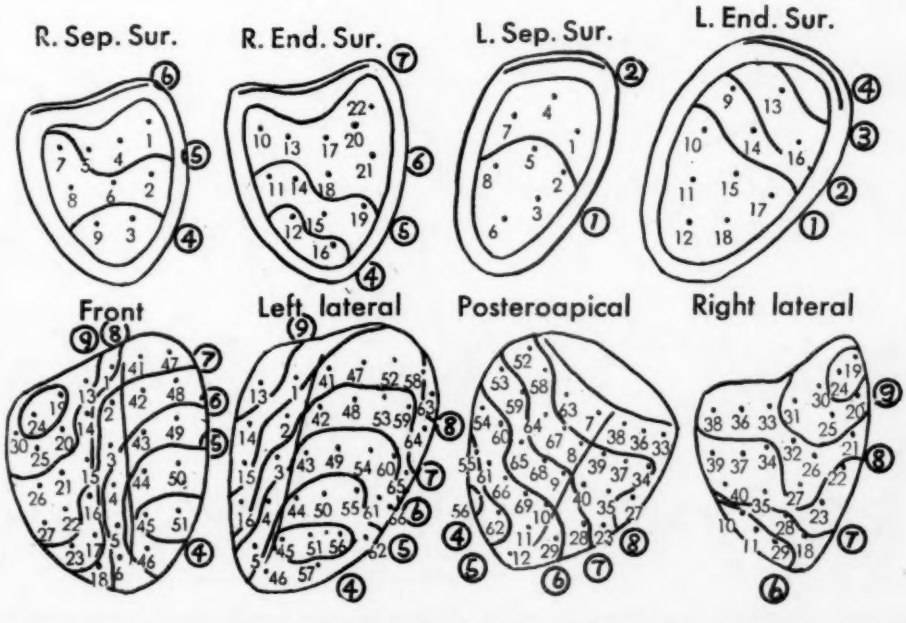

Fig. 9.—Illustration of a pattern of propagation process of ventricular activation in right bundle branch block. The posterior wall of the right ventricle was assumed to be depolarized earlier than the anterior wall of the same ventricle.

Only in posterior myocardial infarction, in which the right posterior as well as the left ventricular muscles were infarcted, was the terminal portion slightly displaced superiorly from its original position, but it still remained inferior to the right anterior.

On the contrary, the initial force and the body of QRS loops were inscribed displacing from their original position of inscription in isolated right bundle branch block. The directions of the displacement of these portions of QRS loops were nearly the same as those in isolated myocardial infarctions. That is, in

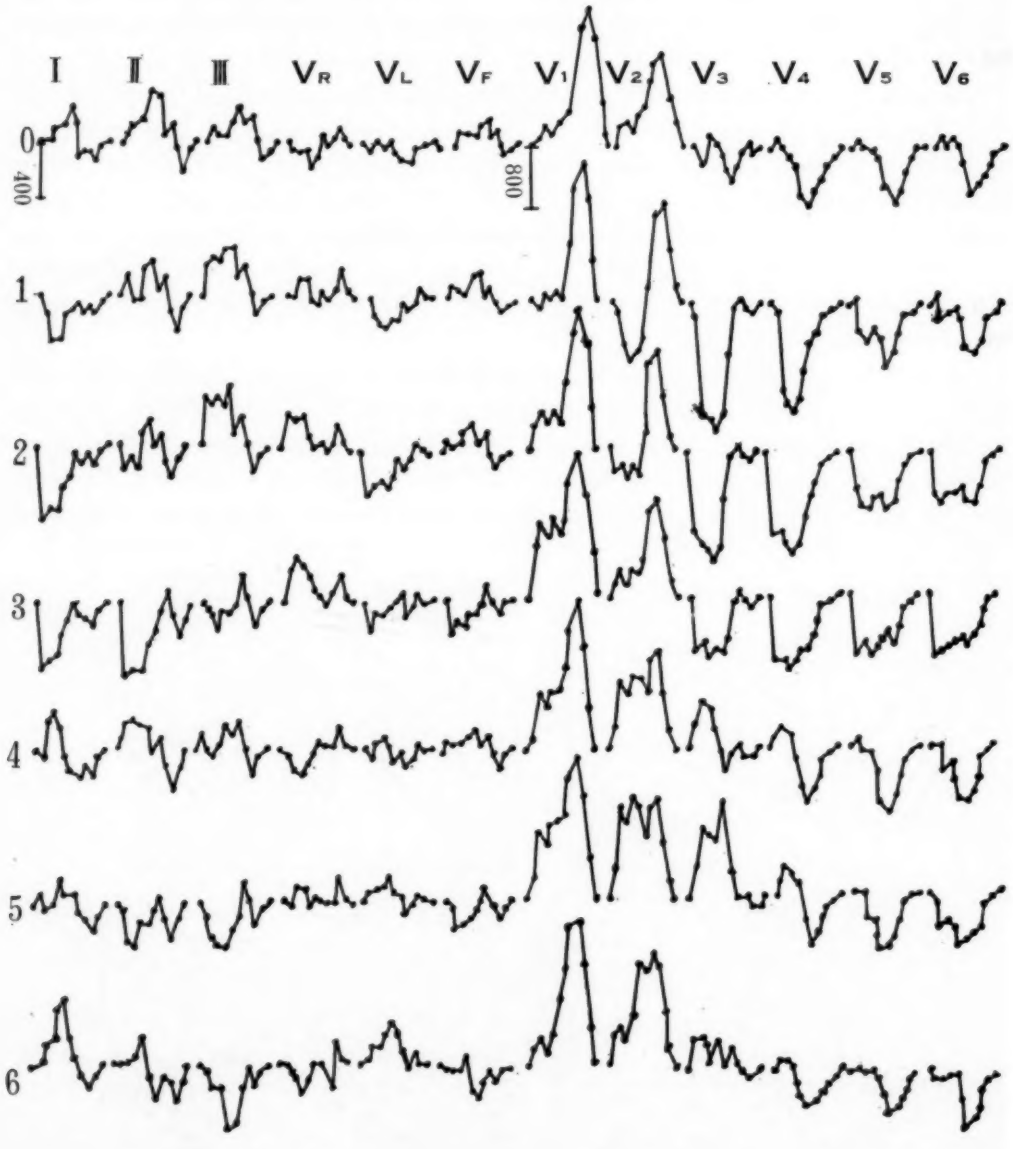

Fig. 10.—Illustration of electrocardiographic changes in right bundle branch block complicated by six myocardial infarctions of different position. The electrocardiograms at the top of the figure are those in uncomplicated right bundle branch block and were reconstructed on the basis of the propagation process illustrated in Fig. 9.

anterolateral infarction the inscribed initial force was displaced to the posterior from its original position of inscription; in anterolateral infarction the initial portion was significantly displaced to the right; and in anteroposterior infarction the initial force and body were displaced distinctly to the right.

In lateral infarction, changes were nearly the same but not so significant as in anteroposterior infarction. In anterolateral infarction the initial portion through the mid-portion was displaced to the right and somewhat anteriorly, and in posterior infarction it was displaced anteriorly to the superior from the original position in isolated right bundle branch block.

The direction of inscription of the QRS loop was variable according to the position of the infarcted area. (Details will be reported elsewhere.)

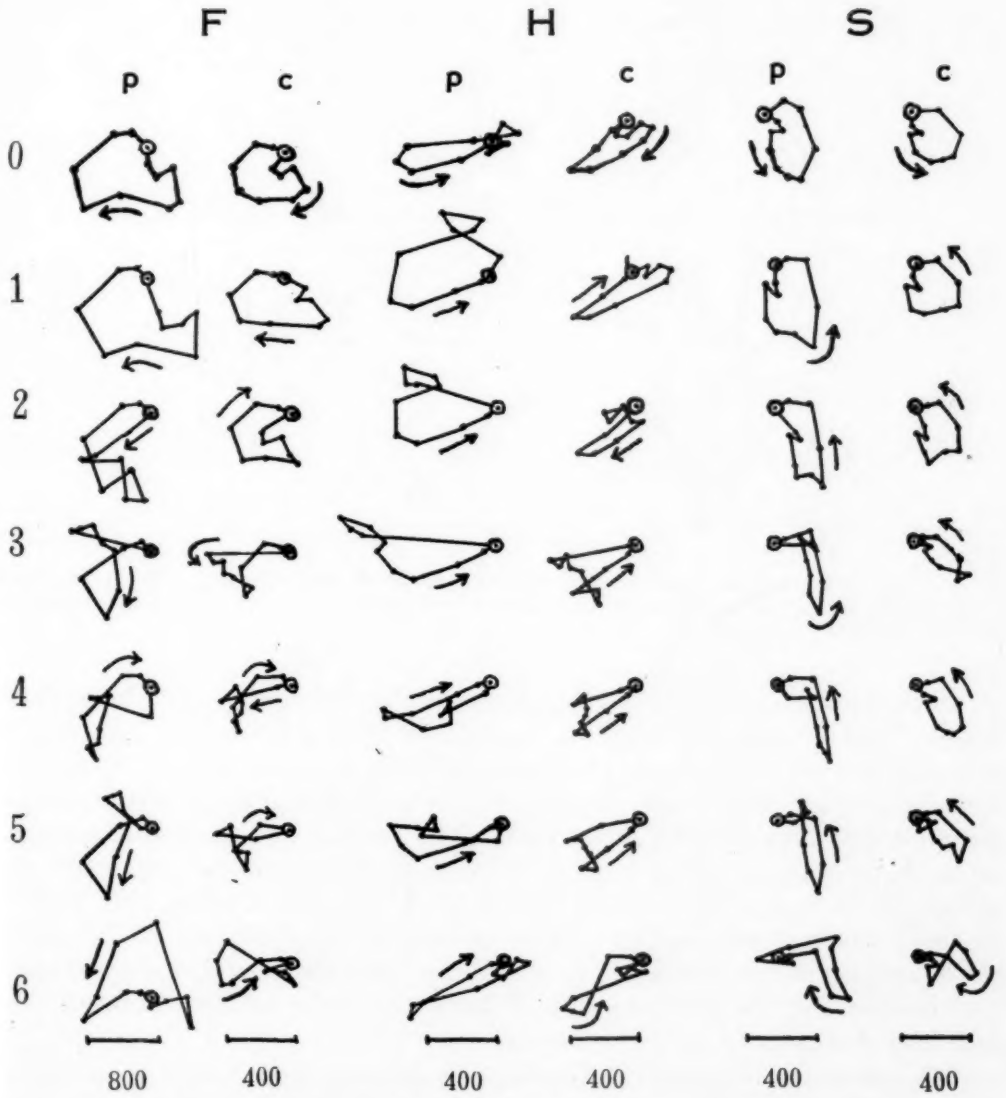

Fig. 11.—Illustration of vectorcardiographic changes for the same electrocardiographic changes, respectively, as shown in Fig. 10.

Electrocardiographic and Vectorcardiographic Changes in Left Bundle Branch Block Complicated by Left Ventricular Myocardial Infarction.—

Electrocardiographic changes: When left bundle branch block was complicated, electrocardiograms of the precordial leads presented no typical changes in comparison with those in uncomplicated left bundle branch block. A Q wave which was characteristically seen in the lead over the infarcted area in uncomplicated myocardial infarction was not observable in any lead over the infarcted area in complicated myocardial infarction.

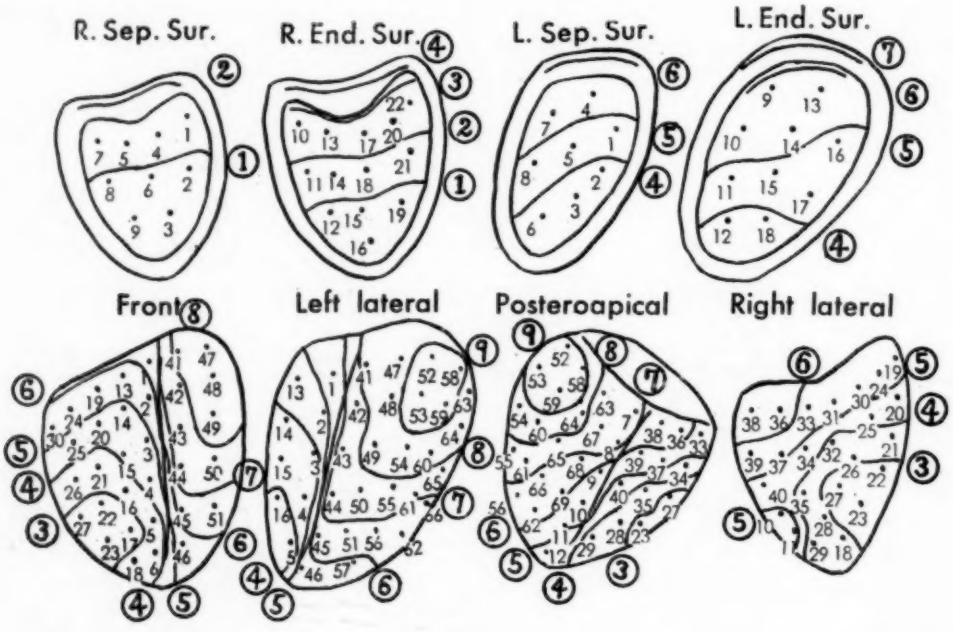

Fig. 12.—Illustration of a pattern of propagation process of ventricular activation in left bundle branch block. The posterior wall of the left ventricle was assumed to be depolarized earlier than the anterior wall of the same ventricle.

The tracings at the top of Fig. 13 are the electrocardiograms in isolated left bundle branch block; the other tracings (rows from 1 through 6) are those in myocardial infarctions complicated by left bundle branch block. The tracings 1 through 6 are, respectively, anteroseptal, anterolateral, anteroposterior, lateral, posterolateral, and posterior infarctions. The location and the size of infarcted areas are the same as in Fig. 1. The propagation process of the ventricular activation in this case of left bundle branch block was that illustrated in Fig. 12. In this pattern of propagation process of ventricular activation the process in the left ventricle was planned in such a manner that the posterior wall was activated earlier than the anterior wall, and the portion activated last was the anterior high lateral portion of the left ventricle.

In every case, myocardial infarction complicated by left bundle branch block was very difficult to differentiate from isolated left bundle branch block, because of the very slight characteristic differences between them. An important finding

is that the reciprocal effect, or tall R waves in Leads V_1 to V_3 seen in isolated posterior and posterolateral infarctions, did not appear in the records of myocardial infarctions of these positions complicated by left bundle branch block.

According to our results, the abnormal pattern of extremity lead electrocardiograms, i.e., concordance of main QRS deflections in Leads I, II, and III, was occasionally observed in infarction of the anterior wall, especially in the event that the anterior wall was activated earlier than the posterior wall in the left ventricle.

Fig. 13.—Illustration of electrocardiographic changes in left bundle branch block complicated by six myocardial infarctions of different position. The electrocardiograms at the top of the figure are those in uncomplicated left bundle branch block and were reconstructed on the basis of the propagation process illustrated in Fig. 12.

Vectorcardiographic changes: Tracings in Fig. 14 illustrate vectorcardiographic changes in the same cases as those in Fig. 13. Tracings at the top of Fig. 14 are the vectorcardiograms in isolated left bundle branch block. The features of these vectorcardiograms in left bundle branch block were scarcely altered by complication of myocardial infarction of any left ventricular position, as can be seen. Therefore, essentially no characteristic change was observable in the vectorcardiogram of left bundle branch block when left ventricular myocardial infarction was complicated.

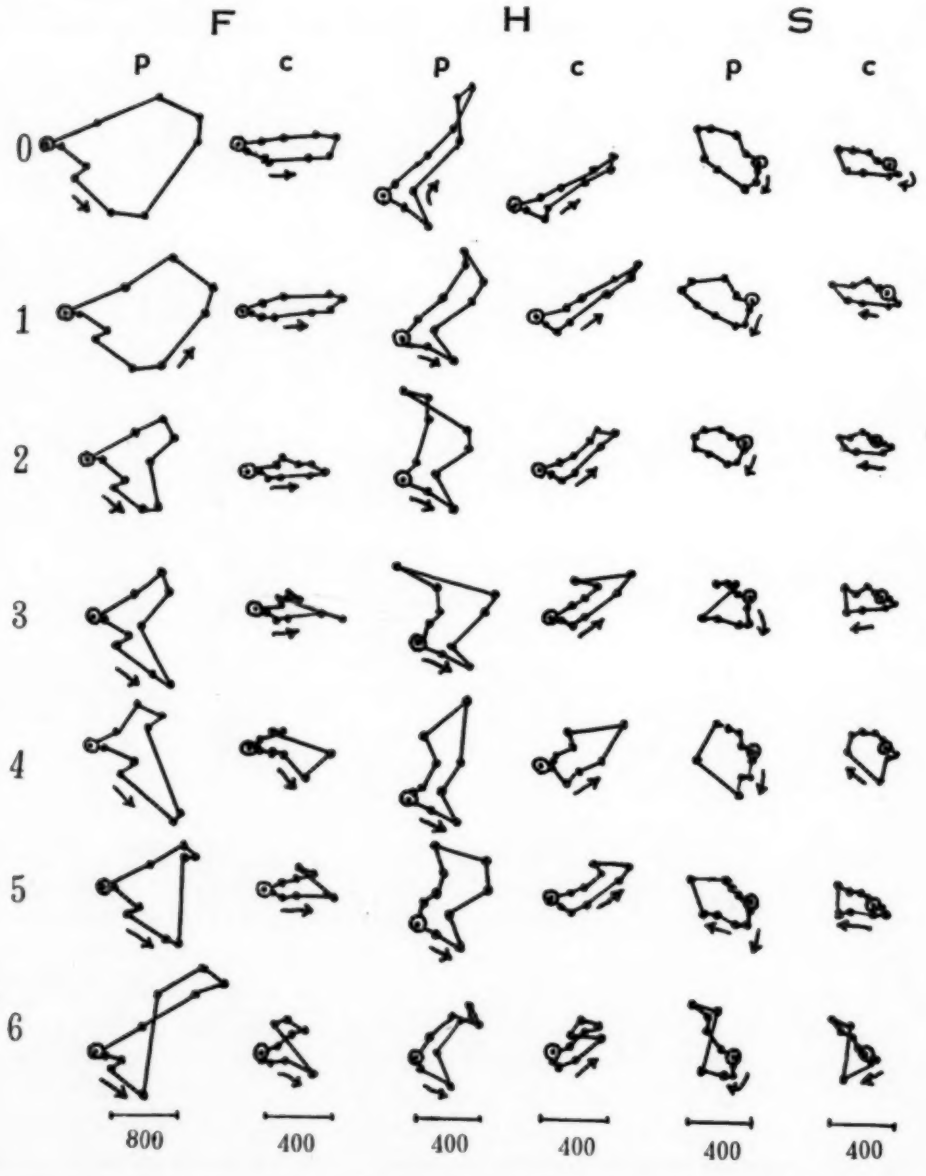

Fig. 14.—Illustration of vectorcardiographic changes for the same electrocardiographic changes, respectively, as shown in Fig. 13.

DISCUSSION

Changes in the electrocardiograms of patients with uncomplicated old myocardial infarction have been reported by Wilson, Myers, Pruitt, Prinzmetal, their collaborators and others,[1-20] and those in the vectorcardiogram by Scherlis, Burch, Elek, their collaborators and others.[21-24,38,39]

According to their results, the most significant change in the QRS complex of the electrocardiogram is the appearance of q or Q wave in leads over the infarcted area. Corresponding change in the vectorcardiogram is represented by displacement of some specific portion of the loop directed away from the infarcted area. The displacement occurs in different portions of the QRS loop, depending upon the position of the infarcted area.

The results of the electrocardiographic and the vectorcardiographic changes obtained by the reconstruction method in the present report agreed excellently with the clinical observations of many other authors. Particularly, the electrocardiographic changes in anterior, anterolateral, anteroposterior, lateral, posterolateral, and posterior myocardial infarctions revealed striking resemblance to those reported by Myers and his co-workers.[10-15]

In model experiments of vectorial representation of the electrical heart axis, we have had the experience that the direction and magnitude of the represented vectors did not show any significant difference in the round, square, rectangular, and oval receptacles of the conductive medium. For this reason the reconstruction method was attempted under the assumption that the human body is an electrically homogeneous medium and the heart is immersed in an infinite homogeneous medium with the same conductivity, that is, in an infinite extensive volume conductor.

In the presence of this assumption, we did not necessarily expect the results of the present study to agree so closely with the experimental and clinical findings of many authors. It may be said that such a good agreement could indicate strong reliability for the reconstruction method, and this method may offer important data pertinent to many unsolved problems in electrocardiography and vectorcardiography.

Commonly, Q phenomenon in the leads over the area of an old infarction has been explained by the concept of an electrical window[40]; that is, the cavity Q wave is transmitted through the electrically inactive region of the infarcted area or the electrical window to a lead-point in the epicardial side over the infarcted area. However, according to the present results, the Q wave in the leads over the infarcted area is not the cavity Q itself transmitted through the window. Strictly speaking, the genesis of the Q wave in the leads over the infarcted area is different from that in the cavity lead.

Normally, the activation is conducted especially early to the septal and endocardial muscles, transmitted by the special conduction system of Purkinje fibers, and then further conducted through the ventricular wall with relatively slow conduction rate from endocardial to epicardial surface. Therefore, the endocardial surface of a transmural infarct is surrounded by the activation wave in the early stage of the ventricular activation in isolated myocardial infarction or in left ventricular myocardial infarction complicated by right bundle branch

block. In this condition of ventricular activation, the electric double layer, generated at the front of the activation wave, takes a saccular form surrounding the septal and endocardial activated muscles, except for the region of the infarcted area, as illustrated in *A* of Fig. 15.

The polarity of this electric double layer is inwardly negative and outwardly positive. In this condition of the equivalent double layer, the potential at a given point P located over the infarcted area is usually negative, because negative potential effect resulting from the opening (*O* in diagram *A* of Fig. 15) of the double layer, broken through at the infarct area, is predominant at that point.

If the activation wave proceeds on farther and the wave front takes a position such as that illustrated in *B* of Fig. 15, the electric potential at the point P will increase still further in its negativity. The larger the extent of infarcted area the broader is the Q-wave zone, and vice versa. As seen in diagrams in Fig. 15, the appearance of the Q phenomena[25] is determined by the condition of the interrelationship between the process of the spread of ventricular activation and the location, the extent of the infarcted area, the position of the lead-point, and some other factors.

However, if the activation should spread in such a manner that the wave front always keeps a rectangular position against the ventricular wall, the Q phenomenon would not appear. For the appearance of the infarction Q, the spread of the wave of activation directed from the endocardial to the epicardial surface may be one of the most important necessary conditions. When the transmural involvement is more complete, the Q p henomenon occurs more readily.

Even though the infarction is transmural, the Q wave will not readily appear in the event that the opposite free ventricular wall has been depolarized at the moment when the muscles adjacent to the infarct area are affected by activation. Absence of a Q wave and appearance of a small R wave in the precordial lead over the infarct area in left ventricular myocardial infarctions complicated by left bundle branch block (Fig. 13) may be cited as a good example of such a case. Many authors have affirmed this finding, in experimental animals and in man, in myocardial infarctions complicated by left bundle branch block.

Wilson and his associates[75] observed in experimental animals and in men that such a Q wave failed to occur when left ventricular myocardial infarction was complicated by left bundle branch block. Similar cases were reported by Kennamer[36] and associates, and Wolff and co-workers.[34] According to Kennamer, in experimental myocardial infarction of the canine heart the pure QS wave seen over the infarcted area changed into a pure R or RS wave after cutting the left bundle branch, and those positive deflections were considerably smaller than those recorded from normal portions of the same ventricle during bundle branch block. This finding agreed quite well with the results in this report.

The reason for this finding is supposed to be as follows: In Fig. 15, when the left bundle is blocked, onset of the left ventricular activation is significantly delayed, and the infarcted area does not keep any direct contact with the front of the activation wave in the early stage of the ventricular activation. Therefore, the potential at a given point P at this instant is due only to the potential effect of the depolarization of the right ventricular muscles.

Since the propagation process of the ventricular activation in the right ventricle in left bundle branch block is nearly the same as in the normal, that is, the course from the anterior wall to the posterior wall in the epicardial aspect, the potential at the point P caused by right ventricular depolarization is almost always positive in the early stage of ventricular activation. It is presumable from the interrelationship between the equivalent double layer at that instant and the position of the lead-point P in *A′* in Fig. 15.

Following this phase, the electrical potential at that point usually increases in its positivity, stage by stage, because the solid angle subtending to the opening of the double layer appearing on the right ventricular epicardial surface tends to increase (*B′* in Fig. 15). As soon as the septal and endocardial surfaces of the left ventricle are affected by activation, the potential at that point usually begins to go down abruptly and changes to negative.

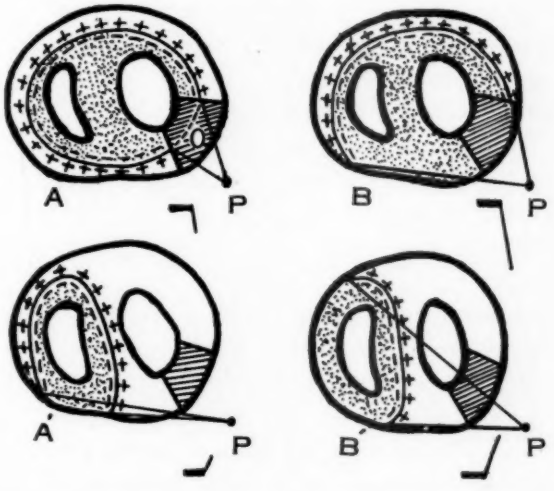

Fig. 15.—A scheme of interrelationships between the ventricular activation process and the potential change in isolated myocardial infarction and myocardial infarction complicated by left bundle branch block. Hatched area indicates the infarcted region, and dotted area, the depolarized region. Mark *O* shows the opening of the electric double layer broken through around the infarct.

For these reasons, the Q wave in the leads over the infarcted area fails to appear in myocardial infarctions complicated by left bundle branch block.

Prominent R waves in Leads V_1 and V_2, and occasionally in Lead V_3, in isolated myocardial infarction are usually known as the reciprocal effect in posterior or posterolateral infarction. According to Levy and associates[37] and Tulloch,[38] prominent R waves in Leads V_1 and V_2, with or without an R wave in Lead V_R, usually occur in posterior or posterolateral old myocardial infarction. The same implication is present in the patient presented by Myers and co-workers.[14,15]

Myers and co-workers,[11,12] Elek and associates,[39] and Grishman and associates[21] reported that prominent R waves in right precordial leads take place only in old infarcts of specific location, such as posterior and posterolateral in-

farctions. Prominent R waves in Leads V_1 and V_2, with or without a tall R wave in Lead V_R, are also reported in patients with old myocardial infarction of lateral or anterolateral position.[37,39]

Elek and associates[39] stated that these prominent R waves occur in a special relationship of the infarcted area to the remaining myocardium, in either antero- or posterolateral wall infarctions. According to the present results, R waves in Leads V_1 to V_3, especially in Lead V_2, became larger in old lateral, posterolateral, and posterior infarctions, and a late R in Lead V_R appeared in old posterolateral infarction. In anteroposterior infarction, the initial R wave became larger only in Lead V_1, and the same tendency was seen also in anterolateral infarction.

Therefore it may be stated that when the problem is concerned with the prominent R wave in right precordial leads, the tall R waves in Leads V_1 to V_3 are most impressive in old lateral, posterolateral, and posterior infarctions, as Levy and associates[37] and Tulloch[38] have said. But, when it is concerned with Lead V_1 alone, the increment of R wave in anterolateral and anteroposterior infarctions is impressive, as in the results of Elek and associates.[39] If these myocardial infarctions are complicated by right ventricular hypertrophy, a more prominent R in Lead V_1 will be expected.

If we interpret this phrase contained in Elek's report, "in the relation of the infarcted area to the remaining myocardium," to mean "in the relationship of the infarcted area to the spread of the ventricular activation," then the occurrence of a prominent R wave in Lead V_1 in anterolateral infarction may also be quite reasonable.

According to our results, the appearance of the initial R or late R in Lead V_R was by no means a common condition of old myocardial infarctions of those positions. It differed according to the location of the infarct.

The late R in Lead V_R was seen in old posterolateral and anteroposterior infarctions and tended to appear in old lateral, anterolateral, and posterior infarctions, depending upon the electrical position of the heart. The initial R tended to appear in old anterolateral and anteroposterior infarctions.

The Q wave in Lead V_F was seen in isolated old posterolateral, posterior, and anteroposterior infarctions. It was, however, not necessarily a complete Q, but was sometimes preceded by a rudimentary or small R wave. The abnormal position of the lead-point of Lead V_F, as reported in results, may be partially responsible for the presence of the preceding small R.

From another point of view, it may be said that the onset of the QRS wave with a complete Q wave in Lead V_F is not always a necessary condition for the presence of posterior or posterolateral old myocardial infarctions. Marked reduction of the initial positivity in Lead V_F may be a warning of old infarction located in these positions.

Variations in the features of extremity lead electrocardiograms in right and left bundle branch block were very attractive as a subject of discussion. However, they will be discussed elsewhere because they are very much complicated and require more study. It is noteworthy that the extremity lead electrocardiograms always displayed the rare type of bundle branch block when right bundle branch block was complicated by left ventricular myocardial infarction of an-

terior aspect. From this finding it may be surmised that the clinical electrocardiogram in right bundle branch block complicated by left ventricular myocardial infarction of anterior aspect will almost always display the rare type of bundle branch block so long as the heart takes the same anatomic position as that used for the measurement of the solid angles in our series of reports.

In regard to the vectorcardiogram of a patient with an isolated old myocardial infarction, it is well known that a portion of the QRS loop is displaced from its original position directed away from the infarcted area. But the portion displaced in the reports of many authors is not necessarily identical. As a reason of such variability in the results, we may propose the difficulty in comparison of features of the QRS loops which were recorded before and after occurrence of myocardial infarction.

In the reconstruction method, however, the comparisons of the QRS loops before and after the occurrence of the infarction are very easy, not only in the general features but also in the partial changes of a given portion of the loop at a given instant. Thus, this procedure allows observation of the QRS loop displacement due to infarction, not only in direction and magnitude, but also in time relations.

In general, changes of the early portions of the QRS complex and QRS loop which occur as results of an old myocardial infarction are well known, but later portions are left in obscurity. According to Burch and associates,[22] the later portions of these complexes also change their features in old posterior myocardial infarction. They said that it was likely that changes in the later portions of these complexes also occurred, but had been neglected. Their statement quite agrees with the results of the present study.

In old posterior and posterolateral infarctions, QRS loop deformation occurred during the period from the second to the seventh stage of the spread of ventricular activation, as seen in Figs. 6*A* and 6*B*, namely, from the relatively early stage to the later stage. During this period, the front of the activation wave in the ventricle always keeps direct contact with the infarcted area.

In the first stage, in which the deformation was not observable, the front of the activation wave had no contact with the area of infarct. In old myocardial infarctions of anterior and anterolateral positions, the front of the activation wave gives up its contact with the infarcted area in a relatively early stage, so that the displacement of the QRS loop occurs only in the relatively early portion of the loop.

On the contrary, almost the entire portion was displaced when an old myocardial infarction of the anteroposterior position was present, because the front of the activation wave tended to keep contact with the infarcted area from the early stage to the later stage.

In general, the subendocardial activation spreads throughout the subendocardial muscles in a relatively early stage of the ventricular activation, by means of the special conduction system of the Purkinje fibers. Therefore, so far as conduction disturbances such as bundle branch block do not occur, the initiation of the QRS loop displacement due to the infarcted area is in a relatively early stage of ventricular activation in myocardial infarction in all locations.

Displacement of the QRS loop due to an old infarct is generally away from the infarcted area. The spread of the ventricular activation from inside to outside is thought to play an important role for the displacement in such a direction.

If the front of the activation wave should spread, always keeping rectangular position against the ventricular wall, the displacement and the general configuration of the QRS loop would not appear in a manner such as mentioned above.

The cause of the displacement of deflection of inscription in the vectorcardiograms and Q phenomenon and/or RS-T depression in the electrocardiograms is, largely, the disorder of polarization and/or depolarization ability of the injured muscle cell membranes. The total effect of these abnormal abilities of the injured muscle cell membranes may be substituted electrically for the abnormality of the electrical moment of their equivalent double layer induced at the boundary between the injured and the uninjured areas.

The membranes of the equivalent electric double layer in fresh infarctions are presumably in one of the following three conditions[18]: (1) membranes completely depolarized by injury and, of course, unresponsive to stimuli; (2) membranes in normal polarization in resting stage but unresponsive to stimuli; (3) membranes partially depolarized in resting stage and unresponsive to stimuli.

We can expect under the first condition the depression of the zero line or T-R interval of the electrocardiograms recorded at a given lead-point P facing toward the injured area, and the elevation of the zero line at a given lead-point P′ behind the injured area. Under the second condition, we can expect the elevation of the RS-T segment at point P, and the depression of it at the point P′. Under the third condition, depression of the zero line and elevation of the RS-T segment at point P, and elevation of the zero line and depression of the RS-T segment at the point P′, may be expected.

In any of these conditions, the relative elevation of the RS-T segment is expected at lead-point P and the relative depression at P′. Thus, the changes of the electrocardiograms and the vectorcardiograms are explicable representatively by the change of the second condition of muscle membranes. With the lapse of time, the muscle membranes in the injured region either succumb or restore their polarization and depolarization abilities, and there appears a new boundary of equivalent electric double layer. The changes of electrocardiograms and vectorcardiograms in such a stage of recovery may be explained by the changes of response ability of the membranes making up a new boundary of equivalent electric double layer. These membranes at the boundary of the injured and uninjured regions restore their depolarization ability gradually and eventually become fully responsive to activation. In this case, of course, the involved muscles within the equivalent double layer are treated as a mere electric volume conductor. The electrocardiograms and the vectorcardiograms in Fig. 16 are those in isolated anterolateral myocardial infarction and were obtained by such a means of calculation.

In both the electrocardiograms and vectorcardiograms the diagrams in the upper row show the cases with immediate changes following the occurrence of infarction. The diagrams in the second row show the changes observable when the membranes restored their depolarization abilities to about 20 per cent of

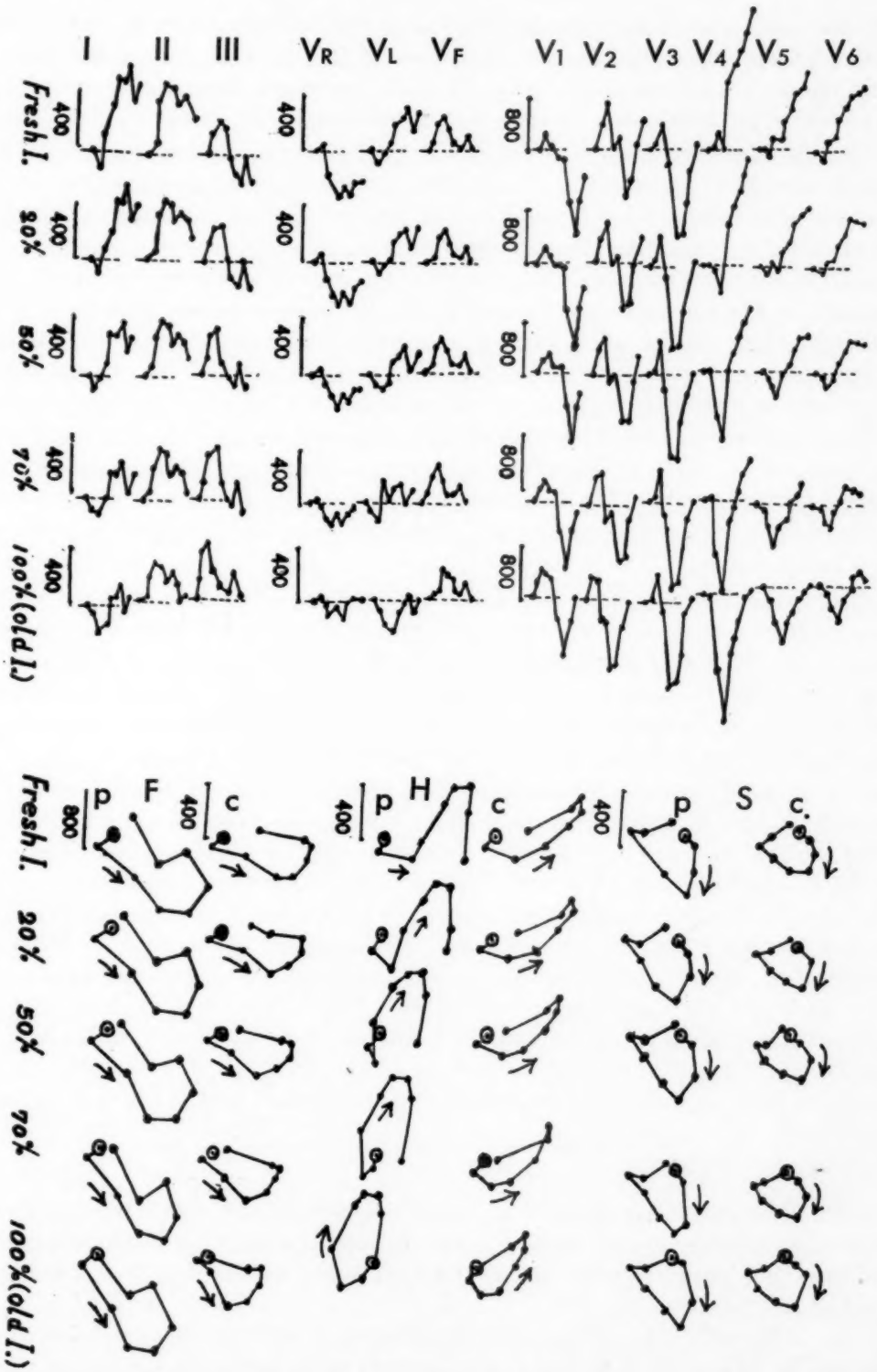

Fig. 16.—Illustration of an example of serial changes of the electrocardiogram and vectorcardiogram in myocardial infarction during progress from fresh to old. The infarct is situated in the anterolateral portion of the left ventricle.

full capacity. The cases in the third row show the changes observable when they restored their depolarization abilites to about 50 per cent, and in the fourth, when restored to about 70 per cent. The lower rows are those in old myocardial infarction after restoration of their full depolarization abilities.

In the electrocardiograms, the RS-T displacements observable in fresh infarction returned gradually to the isoelectric line, Q phenomena appeared increasingly in the precordial Leads V_4 to V_5, and the R wave increased in Lead V_1.

In the vectorcardiograms, the RS-T junction which was displaced toward the infarcted area immediately after the occurrence of infarction, gradually returned to the isoelectric points, and gradually the inscription displacement of a characteristic portion of QRS loop appeared, this displacement being typical of the position of the infarct. These evolutionary changes of the electrocardiograms and/or vectorcardiograms corresponding to the lapse of time conform well to the results of experimental myocardial infarctions reported by many authors.

Some of the vectorcardiograms in old myocardial infarction in the present report closely resembled in configuration the vectorcardiograms of patients with old myocardial infarction presented in the reports of Scherlis, Elek, Burch and their collaborators.

However, as the vectorcardiograms are much more liable to alter in accordance with the changes of the electrical and/or the anatomic positions, and the shape and the propagation process of the activation wave, etc., of the heart, it was very difficult to find clinical vectorcardiograms with features completely identical to those in the present report. But the general tendencies of the changes of the QRS loops were the same as those found by many authors.

From a different point of view, the fact that the results of the electrocardiographic changes in this report were quite similar to those in reports of many other authors may suggest that the changes in the vectorcardiograms obtained by the reconstruction method would be useful as criteria for differential diagnosis. However, it will be necessary to compare the results of this report with those of many other reports which have appeared or will appear in the future. Whether the present results are correct or not may be important to the discussion of whether or not the hypothesis, that a double layer takes place at the boundary between the muscles activated and those at rest, is useful for the explanation of the electrocardiogram and the vectorcardiogram, although there may be many problems to be corrected in the reconstruction method of the present authors.

SUMMARY

1. Electrocardiograms and vectorcardiograms in old and fresh myocardial infarctions of anteroseptal, anterolateral, anteroposterior, lateral, posterolateral, and posterior positions were obtained by means of the authors' reconstruction method.

2. Characteristics of the electrocardiographic and the vectorcardiographic changes in old and fresh myocardial infarctions of these positions were described.

3. Changes in the electrocardiograms and the vectorcardiograms closely resembled those reported by previous investigators.

4. In general, RS-T elevations in fresh infarctions corresponded to Q phenomena or to reduced R waves in old myocardial infarctions; and RS-T depressions in fresh infarctions corresponded to augmentation of R waves in old myocardial infarctions.

5. Displacement of QRS loops directed away from the infarcted area in old myocardial infarctions and displacement of RS-T junctions directed toward the infarcted area in fresh infarctions were the typical changes. These changes were more pronounced in the polyogram than in the vectorcardiograms using the Grishman system.

6. When right bundle branch block was artificially complicated, the Q wave in the lead over the infarcted area in uncomplicated myocardial infarction also appeared distinctly in the leads over the infarcted area. Extremity lead electrocardiograms varied with location and extent of the infarcted area, and every type of right bundle branch block appeared, i.e., the usual and the unusual types of Wilson block and the rare type of bundle branch block.

7. When right bundle branch block was artificially complicated, the initial portion of the QRS loop of the vectorcardiogram was displaced away from the infarcted area, but the terminal portion was scarcely displaced at all in most of the left ventricular myocardial infarctions, and was always inscribed anteriorly to the right.

8. When left bundle branch block was artificially complicated, the Q-wave characteristic of myocardial infarction failed to occur in the leads over the infarcted area, so that diagnosis of myocardial infarction complicated by left bundle branch block was usually very difficult. QRS loops in the vectorcardiogram were not remarkably altered by complication of left bundle branch block. Only the mid-portion of the QRS loop was slightly displaced away from the infarcted area in most cases.

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Spatial Vector Electrocardiography: Method and Average Normal Vector of P, QRS, and T in Space

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In spatial vector electrocardiography the human thorax may be assumed to be a homogeneous sphere with a heart-vector-point source situated at its geometric center. Any heart vector in space may be obtained from its projection in two planes, such as the transcentrally vertical and horizontal planes. The six limb leads define the RLF plane and the six precordial leads define approximately a "horizontal" plane. Furthermore, if it is assumed that the RLF plane and the "horizontal" plane are, respectively, the transcentral vertical and horizontal planes, it is quite convenient to visualize any heart-vector* in space from corresponding polarities written in the routine 12-lead electrocardiogram, by means of lead "polarity" circles concentrically arranged in respective planes. Such an arrangement for the RLF plane from the six limb leads has been previously published by us.[1,2]

METHOD AND ILLUSTRATION

The method is presented in Fig. 1. This figure consists of (*a*) the model, (*b*) the front view of the human thorax with electrodes R, L, F, and six limb lead "polarity" circles, and (*c*) the cross section of the human thorax with precordial electrodes 1, 2, 3, 4, 5, 6, and six precordial lead "polarity" circles. A "polarity" circle is composed of a positive semicircle (white), a negative semicircle (gray), and two zero-potential boundaries.

As can be seen from Fig. 1, *b* and *c*, the polarity circle of a lead is the geometric consequence of the Einthoven assumption. Of a bipolar lead the positive semicircle faces the positive electrode, the negative semicircle faces the negative electrode, and a line joining the two zero-potential boundaries would be perpendicular to that lead axis. Of an unipolar lead the positive semicircle faces the exploring electrode, the negative semicircle faces the Wilson central terminal or the geometric center, and a line joining the two zero-potential boundaries would be perpendicular to that lead axis. Any heart-vector that resides in the positive semicircle yields a positive deflection in that lead, any in the negative semicircle a negative deflection, and any coinciding with a zero-potential boundary a zero potential or a transitional complex.

In Fig. 1, *b* the six concentrically arranged "polarity" circles are, from within outward, those of the limb leads, I, II, III, R, L, and F, respectively. In Fig. 1, *c* the six concentrically arranged

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*Throughout this paper the term "heart-vector" is limited to direction; no magnitude is concerned.

"polarity" circles are, from within outward, those of the precordial leads, $V_{1,2,3,4,5,6}$, respectively. By such an arrangement it is evident that any heart-vector may be visualized at a glance in each plane from corresponding polarities written in six respective leads. At the periphery are given direction marks in degrees, there being 24 in each plane.

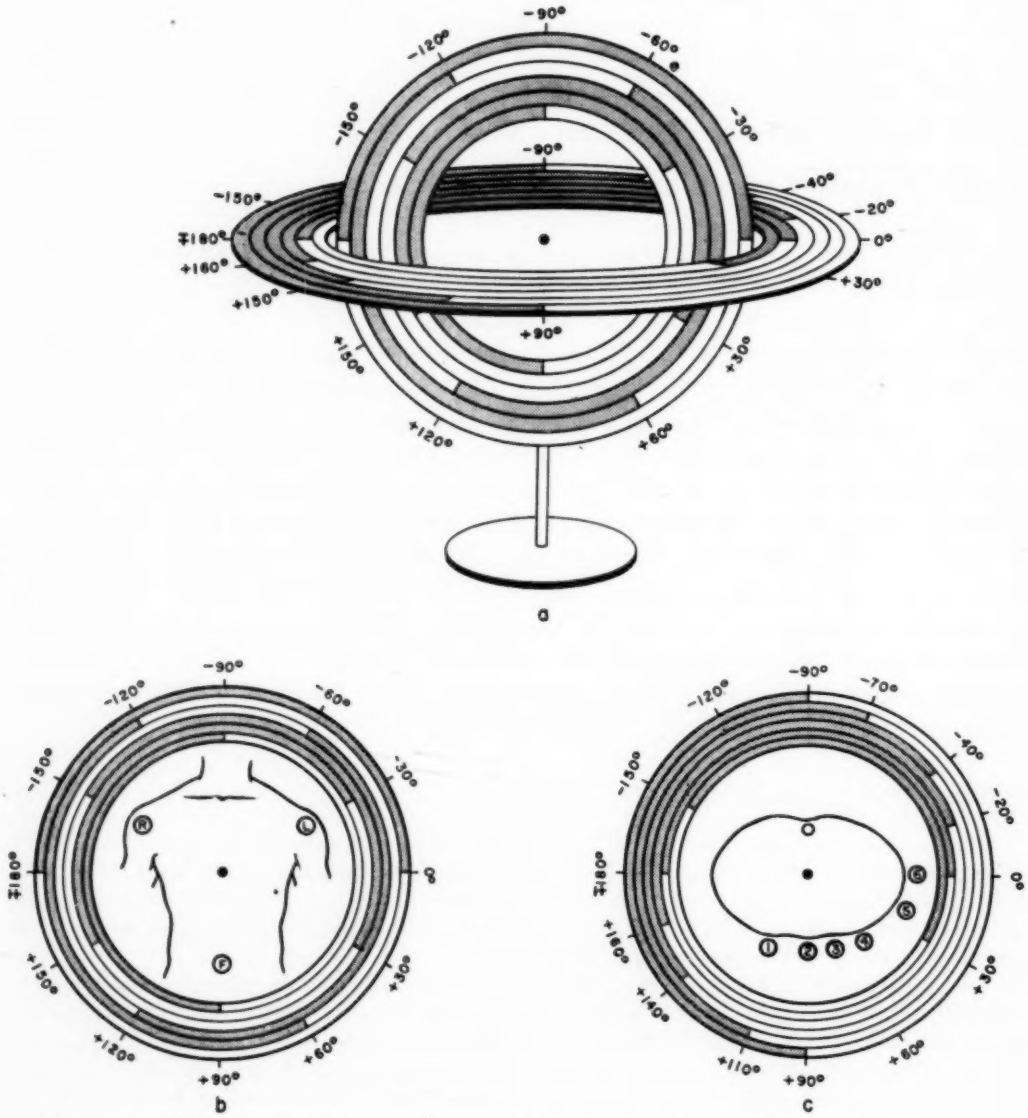

Fig. 1.—The method for spatial vector electrocardiography: *a*, the model; *b*, the RLF plane; and *c*, the "horizontal" plane.

In Fig. 1, *a* the RLF plane and the "horizontal" plane are transposed to the transcentral vertical plane and horizontal plane, respectively. The geometric center represents the heart-vector origin. Any heart-vector in space will cause a vertical plane projection and a horizontal plane projection that can be visually correlated conveniently and rapidly with corresponding polarities written in the six limb leads and in the six precordial leads, respectively, by means of "polarity" circles.

The visual correlation between the vectors of P, QRS, and T in these two planes and the corresponding area polarities written in a normal 12-lead electrocardiogram is illustrated in Fig. 2. In the RLF plane the white arrow indicates the vector of P, QRS, and T; in the "horizontal" plane the white arrow indicates the QRS vector, while the black arrow indicates the vector of P and T.

MATERIAL AND RESULTS

Altogether, 1,000 normal electrocardiograms by the criteria of Frank N. Wilson[3] were selected at random from this laboratory for the present study. All electrocardiograms consisted of 12 routine leads (I, II, III, aV_R, aV_L, aV_F, V_1 through V_6), taken with a direct-writing electrocardiograph.* All patients were over 5 years of age. The vectors of P, QRS, and T were visualized in both planes from corresponding area polarities written in each electrocardiogram. The results are summarized in Table I.

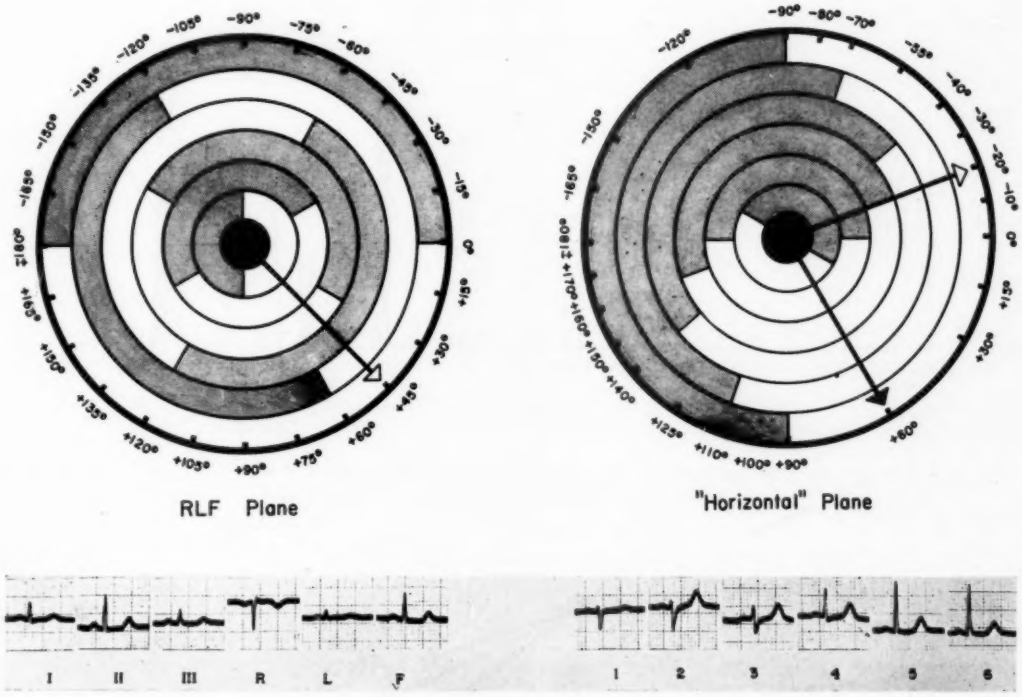

Fig. 2.—An illustration of the visual correlation between vectors of P, QRS, and T in each plane and corresponding area polarities in a normal electrocardiogram by means of the 12-lead "polarity" circles.

The incidence in per cent ($^1/_{10}$ of the actual electrocardiograms) in the various directions of the vectors of P, QRS, and T in both planes is diagrammatically illustrated in Fig. 3.

The average norm of a vector in each plane may be calculated from the formula: $(d_1p1 + d_2p_2 + d_np_n)/100$, in which d is direction, p is per cent. The results are summarized in Table II.

*Sanborn Viso-Cardiette, Sanborn Company, Waltham, Mass.

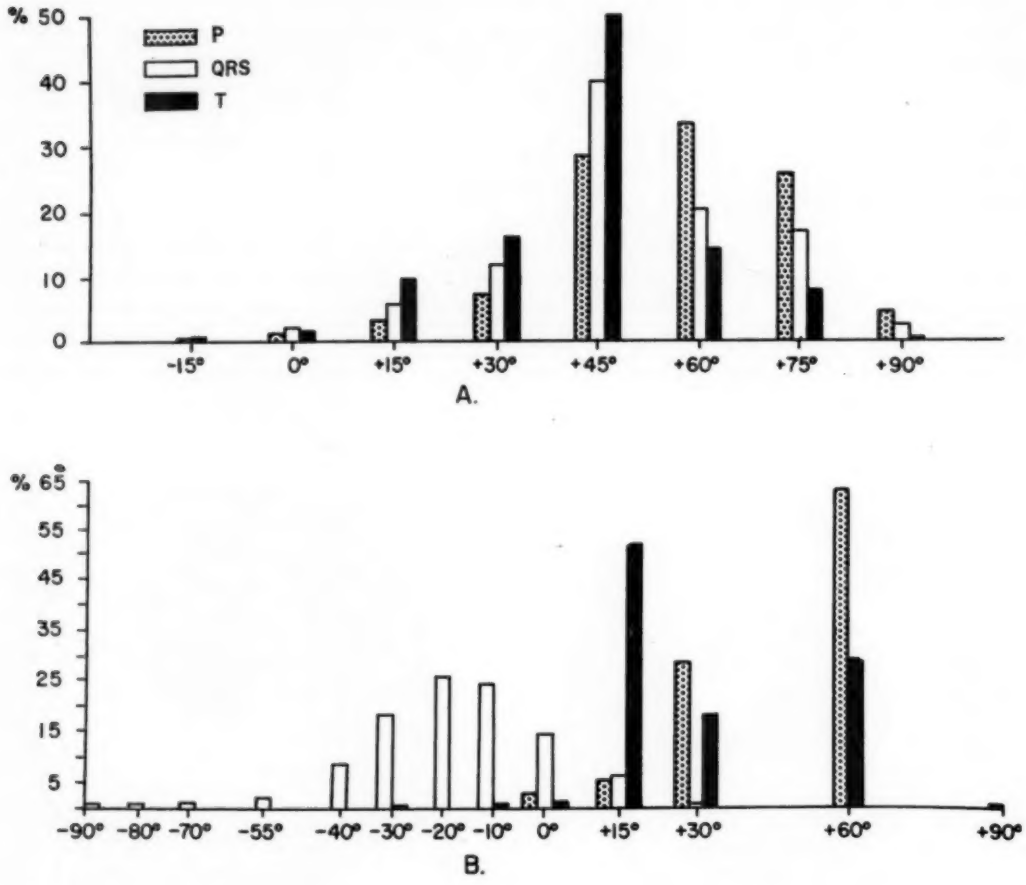

Fig. 3.—The incidence in per cent in the various directions of vectors of P, QRS, and T in the RLF plane (*A*), and in the "horizontal" plane (*B*).

Fig. 4.—The average normal vectors of P, QRS, and T in space.

The front view of the average normal vectors of P, QRS, and T in space is illustrated in Fig. 4. They all point left and downward, P and T being directed anteriorly, and QRS, posteriorly. The angle formed by QRS and T is measured as 60 degrees. The angle formed by P and the plane defined by QRS and T is measured as 15 degrees.

TABLE I. THE INCIDENCE IN THE VARIOUS DIRECTIONS OF VECTORS OF P, QRS, AND T IN THE RLF PLANE AND IN THE "HORIZONTAL" PLANE

RLF Plane

	−15°	0°	+15°	+30°	+45°	+60°	+75°	+90°
P		12	36	74	286	332	255	5
QRS	2	22	60	118	406	196	170	26
T	4	14	97	162	503	138	80	2

"Horizontal" Plane

	−90°	−80°	−70°	−55°	−40°	−30°	−20°	−10°	0°	+15°	+30°	+60°	+90°
P									24	55	288	630	3
QRS	2	2	4	24	87	180	258	239	142	60	2		
T						1		2	10	518	180	289	

TABLE II. THE AVERAGE NORMAL VECTORS OF P, QRS, AND T

	RLF PLANE	"HORIZONTAL" PLANE
P	+55°	+48°
QRS	+47°	−17°
T	+44°	+31°

DISCUSSION

The underlying assumption of the present method is the spatial counterpart of the Einthoven assumption; it, too, is not consistent with real conditions. The human thorax is not a homogeneous sphere; the heart-vector is not centrally located and it is not constantly a single resultant vector as registered in the precordial leads; and the precordial leads do not lie in an absolutely horizontal plane. Real conditions may vary from individual to individual; the inaccuracy of this method, too, is not invariable. This is true of any model with similar underlying assumptions, as for example, the cylindrical model of Grant.[4] In experimental work it has been shown that the amount of inaccuracy obtained from the Einthoven assumption depends each time on its deviation from real conditions and is, indeed, not a matter of more or less careful measurements.[5-7]

The present method is found to be useful as a method for approximate spatial vector electrocardiography from 12 routine leads and in clinical teaching. The

visual correlation between polarities written in the 12 routine leads and the corresponding spatial heart-vector by means of "polarity" circles presents itself as a very practical, convenient, and rapid method of analysis.

The present study is concerned only with heart-vector direction, although spatial heart-vector magnitudes may also be obtained conveniently in this model. For example, one may measure the magnitude of a given vector in limb Lead I; the line which is perpendicular to this lead axis and which cuts this magnitude will intersect the spatial direction of the vector at a point. The point will represent the tip of the spatial vector magnitude. Consequently, this model may be used to reconstruct vectorcardiographic loops in space from a routine 12-lead electrocardiogram. The other laborious or careful methods with similar underlying assumptions cannot, in fact, reduce the inaccuracy.

Real conditions being equal, the inaccuracy of such methods depends furthermore upon the heart-vector direction itself. In an earlier communication we pointed out this dependency, and demonstrated such effect in the frontal plane by means of curves transformed from the Einthoven triangle and the average Burger triangle.[8] It was found that the heart-vector direction obtained in the Einthoven triangle was more inaccurate where the curves were apart, less inaccurate where the curves drew nearer, exceptionally accurate where the curves intersected.

An important concept should be briefly pointed out, namely, spatial vector electrocardiography may be studied on a physically founded basis. By means of a manikin it is possible to obtain Burger lead vectors[9] from the 12 routine leads. It may be anticipated that, on the average, such experimental data when applied to human beings will yield results more nearly accurate than those based merely on the Einthoven assumption or its spatial counterpart. Thus, it seems likely that more nearly accurate spatial vector electrocardiography will be achieved in the near future.

Proper electrode combinations through definite, unequal resistances based on lead-vector data would make it possible to obtain six limb lead vectors in the vertical plane and six precordial lead vectors in the horizontal plane in functional angulation of 30 degrees to each other. This is similar in principle to the functional orthogonalization of vectorcardiographic systems, such as proposed by Schmitt and associates,[10] by Frank,[11] and by us.[12]

In taking the corrected 12-lead electrocardiogram the resistance assembly previously constructed may be inserted between the patient and the electrocardiograph while the electrodes on the patient remain at routine limb and chest positions. The present model (Fig. 1, *a*) may be used for the same purpose after a slight constructive adaptation is made so that a line joining the two zero-potential boundaries of a "polarity" circle will be perpendicular to the same lead vector. We are undertaking this study.

SUMMARY

A method for spatial vector electrocardiography from 12 routine leads by means of a model is described. It is found to be useful as a practical method for quick and approximate determination and in clinical teaching.

Presented are the average normal spatial vectors of P, QRS, and T obtained in this model from 1,000 electrocardiograms classified as normal under the criteria of F. N. Wilson. The average normal vectors of P, QRS, and T in space are directed to the left and downward, P and T being directed anteriorly, and QRS, posteriorly. The angle between QRS and T was 60 degrees; the angle between P and the plane defined by QRS and T was 15 degrees.

The problems of the spatial counterpart of the Einthoven assumption is discussed on the basis of previous experimental work.

It is anticipated that spatial vector electrocardiography may be studied on a physically founded basis by means of the Burger lead-vector concept while the electrodes on the patient remain at the routine 12-lead positions. On the average this will give more nearly accurate results than those based on the spatial counterpart of the Einthoven assumption. The present model may be adapted easily in such study for convenient visual correlation as described above.

We wish to thank Mr. George W. Newman and his staff in the Department of Medical Illustration for making the drawings, and Miss Jennie Selma Wolfer, of the Heart Station, for her valuable technical assistance.

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Renal Adaptations to Postural Changes in Chronic Congestive Heart Failure[1]

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With the Technical Assistance of Joe Yamashita

Among the acute adjustments of the normal human being to the standing position are a decrease in the renal plasma flow (RPF), glomerular filtration rate (GFR), and the urinary rate of excretion of sodium ($U_{Na}V$) and water.[2-4] The same directional changes occur in the supine position with venous congesting cuffs on the thighs, or with phlebotomy, and these effects are prevented by removing the cuffs or giving a transfusion.[5,6] Similar reductions occur in normal subjects in standing exercise,[7-9] but exercise in the supine position causes little change.[9,10] In patients with chronic congestive heart failure, however, exercise in the supine position causes a decrease in these functions,[10] as does standing exercise.[8,9] Congestion of the thighs by occluding cuffs in patients with congestive heart failure in the supine position gives rise to every gradation of response, from the reductions found in the normal patients to a paradoxical increase in RPF, GFR, $U_{Na}V$, and urine flow in certain patients with severe failure.[6]

In the studies on standing exercise in congestive heart failure[8,9] it is not clear whether the changes noted were secondary to position or exercise, or to a combination of these factors. Recently, studies have been done in the tilt position showing a blunting of normal responses.[22] To determine the nature of the renal response to posture alone, 17 patients with chronic congestive failure of various degrees of clinical severity were investigated, and changes in RPF, GFR, $U_{Na}V$, U_KV, $U_{Cl}V$, and water excretion were measured in response to postural changes.

PROCEDURE

In a preliminary study of 4 patients, changing from the supine position to the sitting position with the torso at a 75-degree angle and the legs horizontal on the bed proved to be an inadequate stimulus for changes in the functions studied. The values of all measurements varied only slightly and in an unpredictable manner. Tilting the same patients to 45 degrees on a tilt bed provided a rapid, effective, and reproducible response, and this position was used, therefore, in all experiments reported here.

Seventeen patients who were in chronic congestive heart failure, on the basis of their clinical cardiovascular symptoms and signs, were studied. The experiments were done in the morning

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with the subjects in the fasting state without sedative premedication. All had been on an 800-mg. sodium diet, and none had had mercurial diuretics within 4 days. Because of delayed diuresis in subjects with chronic heart failure, hydration with at least 1 liter of water was begun 18 hours before the experiment. Additional water was given during the procedure on a replacement basis or as tolerated.

Three 10- to 20-minute urine collections were made in the 45-degree tilt position, followed by 3 more in the supine position, and final collections were made again in the 45-degree position, thus bracketing the supine position and allowing each patient to serve as his own control. The experiments were begun and terminated in the 45-degree position because some of the sicker patients were uncomfortable during long supine periods. While in the tilt position, sodium para-aminohippurate was administered intravenously in 5 per cent dextrose in water over a 20-minute period, calculated to give a blood level of 1 to 2 mg. per cent. The flow was then reduced to the rate of 2 ml. per minute in order to maintain constant blood levels. Fifteen minutes were allowed for equilibration. The bladder was then emptied through an indwelling catheter, and at the end of each period it was washed with 30 ml. of distilled water. Air was then injected in 10-ml. amounts, and the residual urine expressed by pressure over the bladder. Six spaced samples of blood were taken in heparinized syringes, using Metycaine for local anesthesia. The cells were separated from the plasma by centrifugation within 1 hour of collection. Blood pressure, pulse, and temperature were determined in each position.

Four normal patients were studied in a similar manner, except that they were hydrated with 1 liter of water 3 hours prior to the experiment and no special diet was given.

The method of Goldring and Chasis[11] with sodium para-aminohippurate was used to determine the RPF. Endogenous creatinine clearances approximated the GFR, the creatinine being determined as described by Peters.[12] It is realized that endogenous creatinine clearance is not always equal to GFR, especially in abnormal subjects, but in short experiments of this nature it is probably a valid measurement of directional changes. Sodium and potassium were determined by the internal standard flame photometer (lithium standard) by the method of White.[13] Chlorides were determined by the potentiometric method of Sanderson.[14] Sodium excretion was not corrected for PAH excretion. It should be remembered that rapid changes in urine flow may produce false apparent change in clearances.

RESULTS

No marked or consistent changes in blood pressure, pulse, or temperature occurred in any patient with change in position. The response of normal persons to tilting has been well documented, and the results obtained in the normal patients in this study, using a 45-degree tilt table, correspond to the generally reported normals.[2-4] This line of investigation was therefore not pursued further and only a small number of normal subjects were studied. Fig. 1 demonstrates the results of an experiment on a patient with chronic congestive heart failure, showing depression of RPF and GFR, decreased excretion of sodium, chloride, and urine, and a reduction of postural changes which occurs in many patients with this condition. Patients studied with the tilt table are shown in Table I in the order of severity of failure.

In the normal subjects tilted to 45 degrees there is a moderate but definite decrease in RPF and GFR, and a more marked decrease in $U_{Na}V$, U_KV, $U_{Cl}V$, and urine excretion. In patients with congestive failure, all measured values are decreased and the positional changes are blunted. Seven of these patients had an almost negligible change in renal function on tilting (E. S., J. J., W. C., F. C., G. C., H. P., and J. B.). Of special interest is G. J., who had a paradoxical increase in values on tilting when in severe failure prior to any treatment (Fig. 2).

TABLE I. TILT AND SUPINE POSITIONS IN NORMAL SUBJECTS AND IN PATIENTS WITH CONGESTIVE HEART FAILURE (IN ORDER OF CLINICAL SEVERITY)

Patient			R.W.	W.N.	E.T.	T.R.	R.C.	M.G.	E.B.	J.J.	F.C.	G.J.‖	J.F.	A.A.	L.N.	E.S.	E.C.	H.G.	E.C.	G.C.	J.B.	W.C.	H.P.	G.J.§
Age			22	46	61	28	50	35	64	58	61	71	56	64	60	63	54	47	66	62	54	63	61	71
Diagnosis*			N	N	N	N	ASHD	RHD	HCVD	ASHD	HCVD	RHD	HCVD	ASHD	ASHD	ASHD	RHD	HCVD	RHD	ASHD	RHD	RHD	ASHD	RHD
Degree of Failure†			—	—	—	—	A	A	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	—
	POSITION	PERIOD‡																						
C_{CR}	45°	1	99	152	—	—	72	176	71	76	78	69	51	41	51	75	49	80	27	35	47	65	44	63
	45°	2	91	160	96	111	86	185	60	79	68	43	53	40	50	73	47	81	24	32	27	70	33	61
	45°	3	86	131	108	93	77	185	65	87	97	35	40	35	51	67	51	53	18	31	—	70	35	60
	Flat	4	97	132	110	115	95	191	89	74	72	63	50	44	40	61	64	73	24	27	50	60	33	48
	Flat	5	105	139	115	114	91	190	85	76	89	57	48	58	66	37	51	73	27	36	38	77	30	48
	Flat	6	106	146	114	116	90	190	75	79	78	72	50	57	59	55	56	85	25	30	46	72	32	55
	45°	7	100	135	—	—	91	184	76	68	75	57	50	51	59	60	34	82	20	34	28	62	33	55
	45°	8	87	140	—	—	72	176	68	84	69	38	42	44	51	86	59	71	27	35	26	72	37	—
	45°	9	—	145	—	—	75	171	62	70	67	35	47	44	—	47	48	60	20	37	62	67	33	62
C_{PAH}	45°	1	650	500	—	—	348	506	291	250	150	262	119	168	165	187	109	132	88	73	146	260	95	184
	45°	2	490	640	436	492	306	470	337	303	152	163	89	149	158	195	119	128	77	68	78	238	89	169
	45°	3	490	492	463	508	342	444	280	335	190	140	98	118	152	168	161	86	61	60	—	240	84	180
	Flat	4	540	502	531	627	435	501	440	274	151	283	117	158	121	155	178	135	75	57	113	200	77	123
	Flat	5	530	420	572	533	475	518	422	278	165	228	105	192	223	89	144	128	84	80	114	260	89	108
	Flat	6	556	485	608	560	470	454	378	274	157	250	143	192	172	125	151	147	83	67	110	233	79	140

	45°	7	498	520	—	—	398	418	330	227	153	202	133	161	180	166	83	136	66	73	75	196	82	144
	45°	8	432	464	—	—	317	428	285	246	148	114	103	153	154	215	171	110	77	72	63	248	102	—
	45°	9	—	385	—	—	361	398	277	244	125	95	119	143	—	127	155	119	64	76	154	208	82	187
Urine (ml./min.)	45°	1	14.1	11.7	—	—	3.3	8.4	5.5	4.6	1.2	1.7	1.9	0.3	3.4	0.6	1.2	2.7	1.6	0.4	0.9	1.5	0.6	1.2
	45°	2	10.4	11.9	2.0	10.7	3.1	8.7	2.4	7.9	1.8	2.3	1.8	0.2	2.9	0.8	0.9	2.4	1.5	0.4	0.3	1.9	0.2	1.4
	45°	3	9.7	10.3	1.3	1.2	2.5	8.6	1.5	8.6	3.2	0.7	1.5	0.1	2.4	0.5	2.1	1.6	1.0	0.4	—	2.1	0.5	1.6
	Flat	4	10.8	7.6	2.9	2.2	3.4	8.8	2.1	7.1	3.3	1.3	2.0	0.2	2.0	0.5	2.7	1.1	1.8	0.3	0.6	1.7	0.4	1.5
	Flat	5	14.2	8.2	8.6	7.2	5.7	9.1	3.0	8.2	5.5	1.7	2.7	0.3	4.6	0.2	2.6	1.3	1.8	0.4	0.4	2.8	0.3	0.5
	Flat	6	15.4	9.5	11.0	10.9	6.7	9.7	3.9	8.0	5.9	3.5	4.1	0.5	5.2	0.3	2.9	2.5	2.2	0.4	0.3	3.8	0.4	0.5
	45°	7	14.7	9.5	—	—	6.2	9.6	2.8	5.0	5.3	4.4	5.0	0.6	6.2	0.3	1.1	3.3	1.7	0.4	0.2	3.4	0.4	0.6
	45°	8	3.5	8.9	—	—	3.1	9.0	1.0	3.4	3.0	1.8	3.1	0.5	4.7	0.6	1.4	2.1	2.1	0.5	0.2	2.4	0.5	—
	45°	9	—	8.1	—	—	1.8	7.7	0.4	2.5	1.6	0.7	2.6	0.4	—	0.4	1.5	1.3	2.5	0.4	1.3	1.7	0.4	1.4
$U_{Na}V$ (μeq/min.)	45°	1	69	198	—	—	26	2.8	49	60	55	25	101	15	31	1.3	3.1	4.1	8.5	3.3	0.9	1.5	0.7	97
	45°	2	27	185	48	34	19	3.0	16	88	45	11	76	4.3	20	1.2	2.9	3.0	6.9	2.1	0.5	1.6	0.7	94
	45°	3	22	164	32	12	15	2.8	9.5	110	39	2.9	47	2.4	12	1.0	1.9	1.8	5.9	1.5	—	1.6	0.7	124
	Flat	4	45	140	59	14	26	3.1	30	66	34	5.2	57	1.7	8.7	1.0	2.9	1.3	7.8	1.2	1.0	1.4	0.7	54
	Flat	5	64	185	119	19	48	4.2	53	87	70	8.7	75	4.2	30	3.1	3.9	1.4	8.7	1.9	1.2	1.7	0.7	26
	Flat	6	89	214	134	27	58	5.3	74	82	106	21	118	12	41	4.0	4.9	2.7	8.7	1.3	1.2	2.7	0.9	30
	45°	7	94	204	—	—	48	4.9	45	78	114	21	132	16	44	4.1	3.2	5.3	8.6	2.5	1.3	6.9	0.9	49
	45°	8	19	153	—	—	19	3.1	24	72	71	7.8	84	7.7	29	3.7	3.7	2.5	9.2	3.0	1.2	5.1	1.0	—
	45°	9	—	127	—	—	13	1.5	—	60	39	4.3	54	2.7	—	4.0	3.8	1.8	5.9	2.1	2.3	5.1	0.8	81

TABLE I. TILT AND SUPINE POSITIONS IN NORMAL SUBJECTS AND IN PATIENTS WITH CONGESTIVE HEART FAILURE (IN ORDER OF CLINICAL SEVERITY) (CONT'D)

Patient			R.W.	W.N.	E.T.	T.R.	R.C.	M.G.	E.B.	J.J.	F.C.	G.J.‖	J.F.	A.A.	L.N.	E.S.	E.C.	H.G.	E.C.	G.C.	J.B.	W.C.	H.P.	G.J.§
Age			22	46	61	28	50	35	64	58	61	71	56	64	60	63	54	47	66	62	54	63	61	71
Diagnosis*			N	N	N	N	ASHD	RHD	HCVD	ASHD	HCVD	RHD	HCVD	ASHD	ASHD	ASHD	RHD	HCVD	RHD	ASHD	RHD	RHD	ASHD	RHD
Degree of Failure†			—	—	—	—	A	A	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	B
U_KV (μeq/min.)	POSITION	PERIOD‡																						
	45°	1	73	61	—	—	29	55	47	19	41	71	56	48	26	35	25	23	4.8	20	2.9	97	31	—
	45°	2	49	79	21	35	29	46	31	19	44	39	52	32	29	38	27	20	4.9	17	14	71	25	70
	45°	3	42	82	21	29	30	41	27	25	55	24	46	26	30	32	30	13	3.3	14	—	61	27	67
	Flat	4	50	73	23	38	29	42	45	20	55	48	59	30	26	26	37	18	4.4	13	17	50	25	47
	Flat	5	74	87	38	40	32	45	56	22	60	52	63	49	39	15	35	17	4.7	19	10	80	24	36
	Flat	6	83	96	39	40	33	49	57	22	53	70	69	69	30	17	39	21	4.9	15	12	92	24	46
	45°	7	88	101	—	—	33	45	43	26	53	62	66	69	36	21	21	22	4.7	20	8.0	91	25	55
	45°	8	45	82	—	—	27	39	31	27	53	31	53	53	32	31	36	16	5.0	20	6.0	121	29	—
	45°	9	—	69	—	—	23	30	27	25	42	20	55	33	—	18	29	14	4.2	19	18	110	25	69

$U_{Cl}V$ (μeq/min.)

	45°	1	—	—	—	—	40	21	45	—	38	—	74	28	25	2.0	4.1	12	—	10	18	91	—	125
	45°	2	—	—	—	35	33	19	20	—	33	—	59	11	21	1.3	4.1	11	—	7	10	65	—	117
	45°	3	27	133	31	22	31	21	13	—	33	—	38	8.5	18	1.0	3.2	5.8	—	5	—	58	—	133
	Flat	4	—	—	—	16	28	24	33	—	29	—	50	8.6	15	1.3	4.8	4.7	—	2	12	45	—	106
	Flat	5	—	—	—	27	47	25	51	—	40	—	53	17	25	2.4	4.7	4.3	—	7	5	66	—	34
	Flat	6	62	173	89	27	48	30	69	—	56	—	87	33	28	3.3	6.4	7.5	—	5	7	85	—	42
	45°	7	—	—	—	—	56	31	50	—	67	—	92	41	35	3.1	4.1	11	—	10	6	90	—	61
	45°	8	39	—	—	—	34	26	28	—	50	—	62	26	27	3.6	5.0	6.7	—	8	5	119	—	—
	45°	9	—	106	—	—	24	18	16	—	32	—	45	12	—	3.5	5.6	5.0	—	5	10	107	—	103

*N = Normal. ASHD = Arteriosclerotic heart disease. HCVD = Hypertensive cardiovascular disease. RHD = Rheumatic heart disease, inactive.

†A = Edema-free on digitalis and low-sodium diet. B = Edema-free on digitalis, low-sodium diet, and intermittent diuretics. C = Persistent edema despite bed rest, digitalis, 800-mg. sodium diet, and frequent diuretics.

‡Each period approximately 15 minutes.

§This patient was in severe failure and was studied prior to any treatment, on Sept. 29, 1955.

‖After treatment with bed rest, low-sodium diet, and digitalis, on Nov. 15, 1955.

When restudied after a 40-pound loss of weight secondary to digitalis and bed rest, he reverted to a normal directional response (Fig. 3), although the general level of function did not increase appreciably.

The difficulty in producing a diuresis in the patients with severe congestive heart failure was striking. Despite forcing fluids for 18 hours prior to the studies,

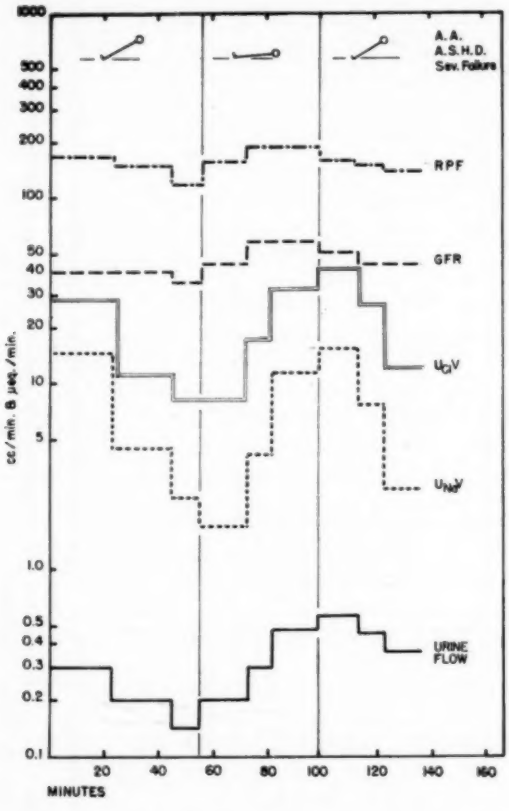

Fig. 1.—Chart of PAH clearance, creatinine clearance, urine flow, and excretions of sodium, potassium, and chloride in a patient with congestive heart failure placed in the flat and 45-degree positions on a tilt bed. The changes are reduced, but in the normal direction.

the rate of excretion of urine was small in some cases. Of the measurements made, changes in sodium excretion were most marked, both in normal subjects and in patients with heart failure. Water, potassium, and chloride excretions generally moved in the same direction, but the responses were smaller.

DISCUSSION

The mechanisms of the renal response to postural change have not yet been completely explained. The antisaluresis and antidiuresis in standing normal subjects can be altered by leg-wrapping and by administration of alcohol, respectively, suggesting at least partially separate mechanisms.[4] Early work describing decreased orthostatic antisaluresis with constriction of the neck indicated

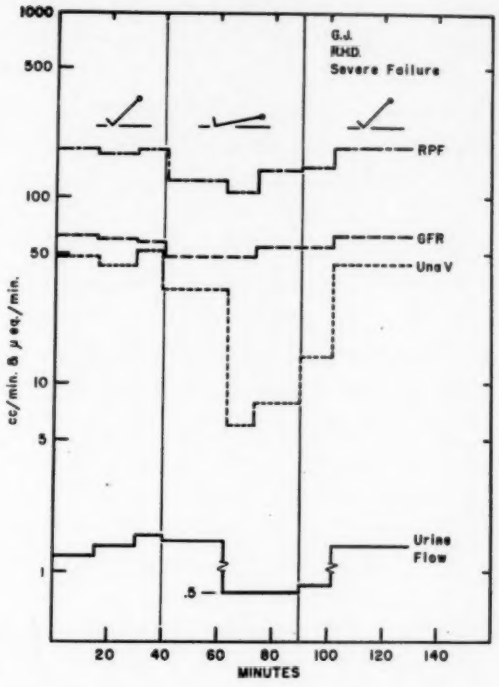

Fig. 2.—Chart of a patient in severe congestive heart failure placed on a tilt bed in the flat and 45-degree positions. There is a paradoxical decrease in functions while flat.

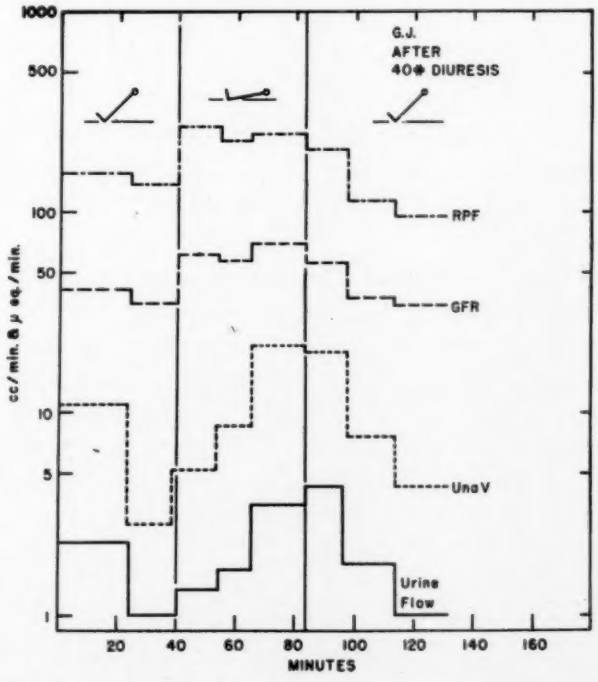

Fig. 3.—Chart of same patient as in Fig. 2, after a 40-pound diuresis secondary to bed rest and digitalis. Postural changes are now in the normal direction.

that control may reside in the cranium, perhaps in a volume-sensitive center,[15] but further studies of neck constriction[16] and the superior vena cava syndrome[17] were not confirmatory.

Cardiac output in normal subjects usually declines in the standing position.[18,19] In supine patients with moderate heart failure, phlebotomy or cuff congestion of the thighs usually causes a decline in cardiac output, RPF, GFR, and sodium and water excretion. In more severe failure, however, these procedures may result in an unchanged or an increased cardiac output, while the renal function may simultaneously increase.[6] Presumably, the total effective circulating blood volume is decreased, and in certain severely failing hearts the cardiac output and renal function are thereby increased.[6,20,21]

The present studies demonstrate directional renal function changes on tilting similar to those observed in congestion of the thighs by occluding cuffs and phlebotomy, but the 45-degree tilt position appears to be a more rapid and effective stimulus. These changes may be mediated by aldosterone, but it is not thought that adequate evidence is presented here on which to base such a mechanism. It can be surmised that in normal subjects and in patients with moderate congestive heart failure, standing reduces the venous return to the heart, and the cardiac output, RPF, GFR, and electrolyte and water excretion are decreased; when these patients are placed again in the supine position, the venous return is increased, and the cardiac and renal functions increase. In cases of severe heart failure, however, the functional phlebotomy produced by standing has essentially no effect on renal function, and it can be surmised that it has no effect on cardiac output, since the heart is working at, or near, its maximum capacity.

SUMMARY

It has been demonstrated that part of the normal human response to standing includes a fall in renal plasma flow (RPF), diminished glomerular filtration rate (GFR), a decrease in the urinary rate of excretion of sodium ($U_{Na}V$), and antidiuresis.

Seventeen patients with chronic congestive heart failure of various degrees of clinical severity were investigated, using a tilt table and alternating between the supine and 45-degree position, measuring changes in renal hemodynamics and electrolyte excretion in response to the postural variations. It was found that patients with a mild degree of congestive failure showed a response similar to normal, with an orthostatic fall in RPF, GFR, $U_{Na}V$, U_KV, and $U_{Cl}V$, and antidiuresis. As congestive failure became more marked, the orthostatic response was reduced, and in certain patients with severe failure there was essentially no response to the tilt position.

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The Effects of "Dry" Heat on the Circulation of Man. I. General Hemodynamics

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That a warm and humid environment imposes certain stresses on the circulation of man has been well established.[1-3,7,9,11] However, no comprehensive hemodynamic data are available which delineate solely the effects of an acute exposure to a warm and relatively dry environment. Such data would afford a point of departure in assessing further studies of the reactions of man to heat under a variety of environmental circumstances.

The object of these experiments was to collect hemodynamic data during the exposure of patients to an ambient temperature of 98°F. ± 1° for 2 hours. The control data were obtained at the comfortable environment of 73°F. ± 1°. The relative humidity was maintained constant throughout at 40 per cent ± 3. A successful attempt was made to prevent changes in hydration through skin and renal water losses by careful intravenous fluid replacement with normal saline solution. The irritability and restlessness which a warm environment is known to produce[2,3] were avoided by adequate sedation. Except for one, the subjects were all individuals with enlarged hearts in whom cardiac disease was caused only by factors which initially burden the left ventricle.

MATERIALS AND METHODS

Sixteen patients were studied, all except one of whom had diseased left ventricles. One group of 8 patients had hypertrophied left ventricles and were not in failure, as arbitrarily judged by a resting wedge pressure of 10 mm. Hg or less (Group 1), except for the one normal subject. The other 8 patients had enlarged left ventricles and were considered still to be in left ventricular failure despite the usual medical measures designed to achieve compensation; these subjects had wedge pressures higher than 12 mm. Hg (Group 2). The causes of left ventricular enlargement were systemic hypertension, aortic insufficiency, and mitral insufficiency. Patients with recent cerebrovascular accidents and obvious coronary disease manifesting as old or recent myocardial infarctions and angina pectoris were excluded.

Following overnight and morning sedation (phenobarbital 0/064 and pentobarbital sodium 0/1, respectively), the subjects were weighed, a 12-lead electrocardiogram was taken, and catheterization of the heart was performed in the postabsorptive state, employing a standard No. 7F

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Cournand catheter. Following the determinations of the central venous and wedge pressures, the tip of the catheter was positioned just within the right pulmonary artery. A No. 19 intra-arterial needle was introduced into the brachial artery of the catheterized arm. The subjects were then transported to the constant-temperature room where they lay comfortably supine on an air mattress, covered only by suitable hand towels for the genitalia and the breasts.

Following a period of stabilization of about 30 minutes in the comfortable environment (73°F. and 40 per cent humidity), the following determinations were made: minute ventilation, respiratory and heart rates, oxygen consumption, cardiac output, mixed venous hematocrit, pulmonary and brachial artery pressures, arterial pH and CO_2 content, rate of finger blood flow, rectal temperature, and skin temperatures from 9 skin points. The room temperature was then elevated to 98°F. ± 1° within 24 minutes, maintaining the humidity at 40 per cent, and repeat determinations were performed at the end of 1 and 2 hours. At this time the catheter was withdrawn, a repeat electrocardiogram was recorded, the patient was reweighed, and the experiment was terminated. All the above determinations were performed in duplicate.

Minute ventilation was measured in a dry gas test meter, expired air was collected in Douglas bags and its oxygen content determined in the Pauling oxygen analyzer. All values were corrected for STP. Blood oxygen contents were determined in a Beckman DU spectrophotometer[6]; arterial CO_2 contents were measured by the manometric method of Van Slyke and Neill[10]; and arterial pH was determined on the Cambridge glass microelectrode apparatus. Arterial pCO_2 was established from the nomogram of Singer and Hastings.[8] The zero point for central venous pressures was 10 cm. from the posterior surface of the thorax in the fourth intercostal space. The pressures were transduced via P23BB and P23D Statham strain gauges and recorded on a Brush DC amplifier oscillographic recorder.

The rate of blood flow in the finger was determined by the venous occlusion technique,[4] and expressed as c.c./5 c.c. of part/minute. Rectal and skin temperatures were observed continuously by means of appropriately shielded iron constantan thermocouples and recorded by a Brown potentiometer.

Left ventricular work, systemic vascular resistance, and total pulmonary resistance were calculated according to standard formulae[5] and expressed as kilogram meters per minute and c.g.s. dyne $cm.^{-5}$ units, respectively.

RESULTS

General data for all 16 patients are presented in Table I. Detailed data for Groups 1 and 2 are presented in Tables II and III, respectively. Average and percentile changes for the two groups and statistical significance analyses (Fisher's T test, groups less than 30) are shown in Table IV.

The average minute ventilation, oxygen consumption, and cardiac index showed slight but not significant increases by the end of the 2-hour period of exposure to heat in both groups. The average arteriovenous oxygen difference and stroke volume showed a slight but not significant decrease. The heart rate increased significantly in both groups. The average respiratory rate did not change in the group with normal wedge pressures; changes in the group with elevated wedge pressures were more difficult to assess because of the initial presence or later development of Cheyne-Stokes respiration in 4 of the patients (see under *Clinical Observations*). The mixed venous hematocrit and body weight remained stable throughout the experimental period.

There was a slight but significant increase in arterial pCO_2 in both groups. Rectal temperature also increased slightly and significantly in both groups, 1.3 and 1.6 per cent, respectively, by the end of the 2 hours. The rate of flow of blood in the finger showed very marked and significant increases in both groups.

TABLE I. GENERAL DATA IN 16 PATIENTS

PATIENT	AGE	RACE, SEX	B.S.	DIAGNOSIS AND CARDIAC STATUS	PRA	PRV	PWP
1. A.C.	44	N F	1.41	HCVD, labile; hypertrophied LV; no failure	1/0 (.37)	18/1 (6.3)	(2.7)
2. J.H.	56	N M	2.22	HCVD; hypertrophied LV; no failure	4/2 (1.9)	30/3 (13.4)	(10.0)
3. E.G.	71	N M	1.62	HCVD "antecedent"; recovered from failure; generalized cardiac enlargement	2/0 (.20)	23/1 (5.3)	(5.3)
4. L.J.	60	N F	1.70	HCVD, slight, labile; slightly hypertrophied LV; no failure	6/4 (3.3)	— —	(8.2)
5. D.C.	43	N F	1.75	Recovered from mild pancreatitis; no heart disease	4/2 (2.5)	25/5 (10.2)	(6.9)
6. G.D.	42	N M	1.76	HCVD; hypertrophied LV; no failure	8/3 (4.8)	33/8 (13.4)	(9.8)
7. S.D.	44	N F	1.68	Predominant systolic hypertension; slightly hypertrophied LV	8/5 (5.6)	29/8 (12.5)	(10.0)
8. W.B.	40	W M	1.66	Mild hypertension, probable coronary sclerosis; enlargement of LV; recovered from failure. BUN 60	5/1 (1.5)	— —	(3.9)

9. N.C.	42	W M	1.66	Rheumatic heart disease; A.I.; M.I.; generalized enlargement; treated congestive failure	5/2 (3.7)	— —	(16.8)
10. G.P.	29	N F	1.55	Rheumatic heart disease; A.I.; enlargement of LV; treated left-sided failure	A.F. (1.3)	26/7 (11.3)	(12.6)
11. J.G.	64	N M	1.42	Syphilitic A.I.; treated left-sided failure	A.F. (2.3)	45/5 (18.4)	(12.7)
12. J.S.	54	W M	1.72	Rheumatic A.I.; generalized enlargement; treated congestive failure	17/9 (9.0)	77/16 (28.2)	(19.1)
13. F.L.	50	N M	1.75	HCVD; enlarged LV; not thought clinically in failure	6/2 (4.0)	51/6 (18.4)	(18.9)
14. W.D.	72	N M	1.62	HCVD; generalized enlargement; treated congestive failure	3/2 (2.3)	40/7 (14.4)	(13.5)
15. J.McK.	64	N M	1.46	Heart disease of unknown cause; generalized enlargement; treated congestive failure	11/5 (8.1)	72/12 (18.4)	(18.1)
16. S.M.	72	N F	1.54	Syphilitic A.I.; generalized enlargement; treated congestive failure	12/9 (9.0)	63/4 (23.0)	(17.2)

B. S. = Body surface in $M.^2$. P_{RA}, P_{RV}, P_{WP} = right atrial, right ventricular, and wedge pressures, respectively. Mean pressures are given in parentheses. Recorded pressures were obtained at the comfortable environment. HCVD = Hypertensive cardiovascular disease. LV = Left ventricle; A. I. and M. I. = Aortic and mitral insufficiency, respectively. BUN = Blood urea nitrogen.

TABLE II. INDIVIDUAL DATA FOR 8 SUBJECTS WITH NORMAL WEDGE PRESSURE (CONTROL LEVELS AND CHANGES AFTER 1 AND 2 HOURS' EXPOSURE TO AMBIENT TEMPERATURE OF 98° ± 1°F.)

PATIENT		P_{PA}	P_{BA}	H.R.	R.R.	VENT./M.^{2}	$BMRO_2$/M.^{2}	A.V.D.	C.I.	S.V.	PU.T.R.	E.T.P.R.	L.V.WK.	pCO_2	RECT. T.°	F.F.
A. C.	C	16/3 (6.8)	139/84 (101.0)	68	16	3.42	81	4.94	1.65	34.2	233	3,467	3.18	44	94.5	0.1030
	1	13/2 (5.3)	122/80 (92.0)	77	16	3.35	104	5.09	2.05	37.5	147	2,548	3.58	46	96.0	3.1456
	2	11/3 (5.1)	102/63 (76.0)	84	16	4.00	114	4.02	2.89	47.7	102	1,518	4.10	50	96.8	4.4683
J. H.	C	28/13 (15.4)	207/122 (145.0)	81	12	3.37	101	4.18	2.42	66.4	229	2,153	10.60	47	96.8	0.1013
	1	21/9 (12.2)	170/108 (122.0)	88	14	3.33	99	4.40	2.25	56.8	195	1,950	8.23	48	97.2	1.0700
	2	17/9 (10.7)	129/83 (97.0)	115	12	3.22	103	4.61	2.23	43.0	173	1,567	6.52	49	97.0	1.4975
E. G.	C	18/9 (10.9)	138/66 (86.0)	83	18	3.52	106	5.52	1.92	37.5	280	2,207	3.62	45	95.6	0.2257
	1	18/9 (11.4)	132/66 (86.0)	81	20	3.72	110	5.66	1.94	38.8	290	2,186	3.65	47	96.5	1.3790
	2	16/9 (9.5)	91/45 (58.0)	85	20	4.01	113	5.20	2.17	41.4	216	1,318	2.75	47	97.0	1.4452
L. J.	C	22/10 (14.5)	154/75 (106.0)	64	24	2.76	100	4.61	2.18	57.8	313	2,289	5.33	40	96.5	0.2299
	1	20/9 (12.4)	128/60 (82.0)	60	cs	2.68	105	4.91	2.14	60.6	273	1,803	4.05	44	96.5	0.9675
	2	20/9 (11.6)	119/59 (79.0)	64	cs	2.75	111	4.74	2.40	63.7	227	1,547	4.38	50	96.5	1.0009
D. C.	C	18/9 (10.7)	109/62 (77.0)	74	16	3.54	118	4.95	2.38	56.2	206	1,480	4.32	46	96.8	0.0868
	1	18/7 (9.2)	93/59 (71.0)	81	16	3.54	126	5.10	2.46	53.2	170	1,315	4.13	48	97.5	1.3416
	2	13/5 (6.8)	73/46 (55.0)	90	16	3.50	118	5.18	2.28	44.4	136	1,100	2.97	48	97.5	1.2888
G. D.	C	22/7 (12.1)	190/120 (147.0)	88	16	3.77	132	4.24	3.12	62.4	176	2,138	10.99	47	96.2	0.0232
	1	17/4 (8.9)	156/92 (116.0)	85	20	3.50	121	3.99	3.03	62.8	133	1,737	8.42	49	96.8	0.6516
	2	16/5 (8.2)	125/75 (95.0)	88	20	3.62	123	3.91	3.14	62.8	119	1,374	7.14	49	97.2	1.3280
S. D.	C	21/10 (13.8)	182/90 (120.0)	68	12	2.70	112	4.38	2.55	63.1	257	2,235	6.95	49	94.2	0.4226
	1	15/9 (10.6)	158/81 (107.0)	75	12	2.71	125	4.00	3.12	70.0	161	1,628	7.58	49	97.2	0.7946
	2	15/9 (10.0)	122/63 (81.0)	83	11	2.86	134	4.10	3.28	66.4	145	1,175	3.79	50	97.5	0.9069
W. B.	C	24/7 (12.7)	147/88 (105.0)	65	16	4.38	138	4.46	3.11	79.3	196	1,628	7.31	41	96.8	0.0274
	1	19/4 (8.6)	136/88 (99.0)	75	16	4.34	137	4.47	3.07	68.0	135	1,551	6.82	42	97.8	0.5900
	2	18/4 (7.6)	109/65 (81.0)	71	16	4.40	141	4.67	3.03	70.8	121	1,287	5.51	44	98.2	0.9977

P_{PA} and P_{BA} = Pulmonary and brachial artery pressures (mean pressure in parentheses). H. R. = Heart rate. R. R. = Respiratory rate (cs = Cheyne-Stokes). Vent./M.^{2} = Minute ventilation in L./M.^{2}/min. $BMRO_2$/M.^{2} = Oxygen consumption in c.c./M.^{2}/min. A.V.D.= Arteriovenous oxygen difference in vol. per cent. C.I. = Cardiac index in L./M.^{2}/min. S.V. = Stroke volume in cubic centimeters. Pu.T.R. and E.T.P.R. = Pulmonary total resistance and systemic vascular resistance in c.g.s. dyne cm.$^{-5}$ units. L.V.WK. = Left ventricular work in kilogram-meters/min. pCO_2 = Arterial pCO_2. Rect. T.° = Rectal temperature in degrees F. F.F. = Finger blood flow in c.c./5 c.c. part/min.

TABLE III. INDIVIDUAL DATA FOR 8 PATIENTS WITH ELEVATED WEDGE PRESSURE (CONTROL LEVELS AND CHANGES AFTER 1 AND 2 HOURS)

PATIENT		P_{PA}	P_{RA}	H.R.	R.R.	VENT./M.^{2}	$BMRO_2$/M.^{2}	A.V.D.	C.I.	S.V.	PU.T.R.	E.T.P.R.	L.V.WK.	pCO_2	RECT. T.°	F.F.
N. C.	C	56/26 (31.6)	142/73 (98.0)	77	cs	3.32	97	7.38	1.29	27.9	1,176	3,665	2.88	46	96.0	0.0224
	1	29/11 (16.0)	116/58 (78.0)	75	cs	2.94	98	7.64	1.28	28.2	604	2,962	2.26	45	96.5	0.5334
	2	26/13 (15.5)	102/49 (68.0)	87	cs	3.16	111	7.16	1.56	29.7	480	2,122	2.40	49	97.5	1.1096
G. P.	C	21/13 (16.1)	147/27 (67.0)	81	24	4.19	117	7.01	1.67	32.0	495	2,049	2.35	45	95.0	0.1563
	1	14/7 (9.9)	109/26 (55.0)	79	20	3.34	102	6.91	1.48	28.9	346	1,923	1.71	52	95.2	0.6748
	2	12/6 (8.4)	92/22 (44.0)	83	23	4.11	122	6.98	1.76	32.7	246	1,291	1.63	52	97.0	1.0169
J. G.	C	44/23 (31.0)	127/60 (82.0)	105	cs	5.28	148	6.96	2.12	28.7	821	2,173	3.26	55	95.5	0.0157
	1	41/20 (26.0)	116/51 (70.0)	109	cs	5.25	144	6.40	2.25	29.2	652	1,755	3.03	55	96.2	0.8502
	2	39/19 (26.0)	106/53 (70.0)	115	cs	4.64	137	6.48	2.12	26.2	691	1,859	2.86	52	96.9	1.4359
J. S.	C	76/31 (44.0)	111/37 (62.0)	84	24	5.25	150	6.65	2.26	46.2	906	1,277	3.27	35	96.5	0.1189
	1	73/28 (41.0)	103/33 (56.0)	89	26	5.55	169	6.48	2.60	53.6	732	1,000	3.41	39	99.3	0.8103
	2	62/20 (34.0)	90/27 (43.0)	96	26	5.85	177	6.68	2.65	47.4	597	755	2.66	40	99.5	0.8469
F. L.	C	45/20 (30.0)	192/103 (135.0)	60	16	2.74	111	4.07	2.72	79.4	503	2,263	8.75	48	95.0	0.0955
	1	29/9 (16.0)	148/71 (108.0)	63	cs	2.83	108	4.45	2.44	67.8	300	2,023	5.21	53	96.5	1.0421
	2	30/10 (17.0)	110/68 (80.0)	66	16	2.88	106	3.99	2.68	71.0	290	1,364	5.06	55	97.2	2.2552
W. D.	C	42/16 (25.0)	138/79 (100.0)	83	20	4.24	140	6.14	2.20	44.5	540	2,162	5.03	50	96.0	0.4860
	1	30/14 (21.0)	145/89 (105.0)	85	23	5.36	144	6.34	2.19	43.4	455	2,273	5.27	50	96.8	0.7104
	2	28/13 (18.0)	107/63 (75.0)	90	24	5.65	151	7.06	2.07	38.5	415	1,727	3.54	52	97.5	1.0140
J.McK.	C	84/35 (50.0)	191/87 (132.0)	100	26	5.23	152	7.41	2.06	30.1	1,328	3,506	5.40	51	97.2	0.0505
	1	57/26 (35.0)	177/80 (123.0)	110	32	5.79	155	7.12	2.18	29.0	877	3,084	5.33	50	97.5	0.6577
	2	42/22 (29.0)	149/74 (105.0)	103	28	5.32	148	6.62	2.23	31.7	710	2,572	4.66	54	97.9	0.6924
S. M.	C	60/30 (40.0)	116/56 (73.0)	72	20	3.72	97	8.10	1.18	26.0	1,709	3,112	1.86	40	97.2	0.0456
	1	60/28 (39.0)	110/51 (70.0)	71	cs	3.64	101	8.31	1.22	26.3	1,670	2,996	1.78	42	97.5	1.3913
	2	54/25 (36.0)	83/40 (52.0)	75	22	3.96	103	7.50	1.64	33.6	1,140	1,647	1.78	42	97.5	2.1781

For key to abbreviations see Table II.

The rise in the temperatures of the skin preceded that of the rectum and proceeded at different rates for the various areas studied. These observations will be reported in detail elsewhere.

There was no significant difference in response between the two groups in any of the above parameters.

The most interesting changes occurred in the pulmonary and brachial artery pressures and the calculated resistances and estimated left ventricular work. All subjects with normal wedge pressures showed a decrease in systolic and mean pulmonary artery pressure, and 6 of the 8 showed a decrease in the diastolic pressure. In the 8 subjects with an elevated wedge pressure there was a decrease in the systolic, mean, and diastolic pressures in every instance. The average decrease in mean arterial pressure was statistically significant in both groups. Although the percentile changes were similar for the two groups, the subjects in Group 2 showed a significantly greater decrease than those in Group 1. This reflected the much higher control pulmonary artery pressures in the patients considered to be in left ventricular failure. All patients in both groups showed significant decreases in the systolic, mean, and diastolic brachial artery pressures. There was no significant difference between the two groups.

As a result of these decreases of pressure in the absence of a significant change in the cardiac output, significant decreases were registered in the total pulmonary and systemic vascular resistances of all subjects. As in the case of the pulmonary artery pressures, a significantly greater decrease in total pulmonary resistance was noted in the patients with elevated wedge pressures, again reflecting the much greater initial resistance calculated for these subjects.

The pattern of decrease in the pulmonary and brachial artery pressures was also of interest. In the majority of the patients a definite decrease was

TABLE IV. AVERAGE ABSOLUTE [illegible] PERCENTILE

	P_{PA}	P_{BA}	H.R.	R.R.	VENT.	$BMRO_2$	A.V.D.	C.I.
				Normal Wedge Pressure				
C	12.1	111.0	74	16	3.43	111	4.66	[illegible]
1 hr.	9.8 — 19.0%	97.0 — 12.6%	78 + 5.4%	16 0.%	3.40 — 0.9%	116 + 4.5%	4.71 + 1.[illegible]	[illegible]
2 hr.	8.7 — 28.1%	78.0 — 29.7%	85 + 14.7%	16 0.%	3.54 + 3.2%	119 + 7.2%	4.55 — 2.[illegible]	[illegible]
P(C vs 2 hr.)	< .001	< .001	< .05 > .02	— —	< .4 > .3	< .2 > .1	< .5 > [illegible]	[illegible]
				Elevated Wedge Pressure				
C	33.5	93.6	83	—	4.25	126	6.71	[illegible]
1 hr.	25.5 — 23.9%	83.1 — 11.2%	85 + 2.4%	—	4.34 + 2.1%	128 + 1.6%	6.71 0	[illegible]
2 hr.	23.0 — 31.3%	67.1 — 28.3%	89 + 7.2%	—	4.45 + 4.7%	132 + 4.8%	6.56 — 2.[illegible]	[illegible]
P(C vs 2 hr.)	< .001	< .001	< .01 > .005	—	< .4 > .3	< .3 > .2	< .5 > [illegible]	[illegible]
				Significance Comparison Between the Control and 2-Hour Changes of the Two Groups				
	< .001	< .4 > .3	< .2 > .1	—	< .8 > .7	< .8 > .7	< .9 > [illegible]	[illegible]

first noted at the end of 30 minutes' exposure to heat. This was followed by a progressive and rather steady decrease in the ensuing 60 minutes, and either little change or a further slight decrease in the last 30 minutes.

The changes in left ventricular work, although showing significant decreases, were not as remarkable as the changes observed in the pressures and resistances. Among the subjects with a normal wedge pressure, Patient A. C. showed a progressive increase in work of the left ventricle, and Patients E. G. and S. D., although demonstrating an ultimate decrease, had slight increases at the end of the first hour, as did Patients J. S. and W. D., who had elevated wedge pressures.

Clinical Observations.—Cheyne-Stokes respiration developed in only one subject in Group 1 (L. J.) and persisted throughout the entire period of exposure to heat. Among the patients in Group 2 it was initially present in N. C. and J. G., and persisted unaltered to the end of the experiment. It developed transiently in F. L. and S. M. but disappeared in both before the end of the experiment. Râles did not develop when initially absent, nor did they increase in those subjects in whom they were initially present. Visible perspiration was absent in most and only slight in a few patients. Patients A. C. and S. D. in Group 1, and J. S. and S. M. in Group 2 developed moderate irritability and restlessness; interestingly, they also tended to show definite increases in the cardiac index. The remaining 12 subjects either dozed or lay quietly throughout the entire procedure. This was in sharp contrast to the irritability which developed in the investigators themselves who were forced to be physically active throughout the entire procedure. The postexposure clinical electrocardiograms showed no remarkable change in either group, except for the heart rates, when compared to the control records. However, in Patients J. H. and F. L. in Group 2, who

RCENTILE CHANGES FOR THE TWO GROUPS

A.V.D.	C.I.	S.V.	PU.T.R.	E.T.P.R.	L.V.WK.	pCO_2	RECT. T.°	F.F.
				Normal Wedge Pressure				
66 71 + 1.1 55 − 2.6 < .5 >	42 50 + 3.3% 67 + 10.3% < .2 > .1	57.1 56.0 − 1.9% 55.1 − 3.5% < .7 > .6	236 188 − 20.3% 155 − 34.3% < .001	2200 1840 − 16.4% 1361 − 38.1% < .01 > .001	6.54 5.81 − 12.6% 4.64 − 29.0% < .02 > .01	45 47 + 4.4% 48 + 6.7% < .02 > .01	95.9 96.9 + 1.0% 97.2 + 1.3% < .01 > .005	0.1525 1.2424 + 715% 1.6167 + 961% < .01 > .005
				Elevated Wedge Pressure				
71 71 0 56 − 2.5 < .5 >	94 85 + 0.5% 99 + 7.7% < .1 > .05	39.3 38.3 − 2.5% 38.8 − 1.2% < .8 > .7	935 704 − 24.7% 571 − 38.9% < .001	2526 2252 − 10.8% 1667 − 34.0% < .001	4.10 3.50 − 14.6% 3.07 − 25.1% < .05 > .02	46 47 + 2.2% 49 + 6.5% < .001	96.0 96.8 + 0.8% 97.5 + 1.6% < .001	0.1239 0.8338 + 573% 1.3299 + 973% < .001
				Significance Comparison Between the Control and 2-Hour Changes of the Two Groups				
< .9 >	< .6 > .5	< .9 > .8	< .001	< .9 > .8	< .3 > .2	< .9 > .8	< .6 > .5	< .8 > .7

among others had a marked left ventricular strain pattern in the left precordial leads, the strain pattern was greatly diminished at the end of the experiments. Both of these patients had marked decreases in calculated left ventricular work.

DISCUSSION

The exact effect of a limited acute heat stress upon the systemic blood pressure, the oxygen consumption, and the cardiac output of man has been difficult to assess from a study of previous reports.[1-3,7] This appears to be due to the superimposition of two variables upon the basic increase in the ambient temperature. First, the humidity generally has been concomitantly increased to levels which would interfere with proper heat dissipation and, hence, produce an excessive increase in body metabolic rate. Second, it is evident that most of the subjects for whom data are available were sufficiently uncomfortable that it was not possible to obviate the effects of restlessness and increased motor activity. As a result, these studies have demonstrated either no change or a rise in the systemic systolic pressure[1-3] and in the oxygen consumption,[1,3] and an increase in the cardiac output and the work of the heart.[1,3]

When these two variables are adequately controlled, as in the present experiments, by maintaining the humidity low and by minimizing restlessness and increased motor activity, there is virtually no change in the minute ventilation, the oxygen consumption, and the cardiac output. The sole effects of a profound vasodilatation then become evident, as exemplified by consistent and, at times, profound decreases in the systolic and diastolic systemic pressures and in the systemic vascular resistance. It is of interest that these decreases are likewise noted in the cardiopulmonary bed, both in the subjects with normal* and in those with elevated central venous pressures. Since the cardiac output remains virtually unaltered, this raises the possibility, contrary to previous opinion,[1,7] that vascular resistance in the "internal" territories may also undergo a decrease.

It is likewise noteworthy that, with the exceptions mentioned, the calculated work of the left ventricle usually decreased. This is in sharp contrast to the marked rise in heart work which occurred in the patients studied by Burch and Hyman.[3] In their patients a deliberate effort was made to impose a very uncomfortable stress upon the circulation by the application of temperature and humidity elevations to 111°F. and 86 per cent, respectively; the effects were obviously deleterious, particularly in those patients with congestive failure. Not only was this not the case in the present experiments, but one might almost be tempted to ascribe a beneficial effect of such short-term "dry heat" exposure, particularly for those patients who had left ventricular failure.

In the face of a lack of any significant change in the cardiac output, the basis for the foregoing statement would lie in the following events: (1) A decrease in total systemic resistance, particularly in diastolic hypertensive patients. (2) A decrease in pulmonary artery pressure and total pulmonary resistance. It is of

*Although these pressure decreases are slight, they are considered to be of more than chance significance. Previous studies in this laboratory, wherein pulmonary artery pressures have been recorded serially for 2 to 3 hours in normal subjects with a comfortable environment, have shown small cyclic rises and falls in pressure, rather than a progressive fall.

particular note that this occurred even in the two subjects (J. S. and J. McK.) who were also in right ventricular failure. (3) A decrease in the calculated work of the left ventricle. (4) Failure of abnormal left precordial electrocardiographic leads to undergo further abnormal alterations, and an actual lessening of the deranged ST-T pattern in two instances.

Complete validity for the statement ascribing beneficial effects to the procedure, however, would necessarily depend on the following circumstances: (1) A demonstration that this experimental environment produces no significant decrease of blood flow in the renal, splanchnic, coronary, and cerebral vascular beds, and a significant decrease in their respective resistances. (2) The ability to prevent irritability and increased motor activity, coupled with maintenance of the recumbent position. (3) Prevention of a significant disparity between increased body metabolism and heat dissipation. Even with the precautions that were taken this was not entirely possible, as evidenced by the increased arterial pCO_2 and the slight but definite increases in rectal temperature. (4) Proper maintenance of salt and water balance.

It would be interesting to speculate on the exact mechanism producing the decreases in systemic and total pulmonary resistances, but the present data can offer no self-contained explanation. The same may be said of the production of Cheyne-Stokes respiration not initially present in 3 of the patients, a phenomenon which would here imply some direct or indirect influence of the warm environment upon the respiratory center, quite dissociated from any obvious circulatory change.

SUMMARY

Sixteen patients, 8 with and 8 without left ventricular failure, were subjected for 2 hours to an ambient temperature of 98°F. and a comfortable humidity of 40 per cent. The combination of a low humidity and adequate sedation generally prevented the occurrence of restlessness and increased motor activity.

Neither group of subjects showed any significant change in minute ventilation, oxygen consumption, arteriovenous oxygen difference, and cardiac output. Both groups showed significant decreases in brachial and pulmonary artery pressures, systemic and total pulmonary resistances, and left ventricular work.

It is speculated that the short-term exposure to a warm, dry environment under circumstances which produce the above changes is not deleterious, but may actually be beneficial to certain patients with left ventricular failure.

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The Functional Activity of the Human Conjunctival Capillary Bed in Hypertensive and Normotensive Subjects

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The intermittent nature of blood flow through the peripheral vascular bed of man and animals has long been recognized, being clearly described by Luedde[1] in the first major account of conjunctival microscopy in systemic disease. Following the careful studies of Clark and Clark[2] and others using skin chamber and mesenteric vessel techniques, this intermittent nature of blood flow through the capillary bed became recognized as an essential feature of the blood vascular system, allowing extensive local modifications of peripheral blood flow in response to changed physiologic or pathologic conditions.

To this phenomenon of intermittent peripheral vascular activity, the term "vasomotion" was designated. The definition of vasomotion covers variations in the speed of peripheral blood flow, alterations in caliber of individual vessels, and alternation between activity and inactivity of the capillaries; all of these features arise from apparently spontaneous contraction and relaxation of vascular smooth muscle. It was reported by Clark and Clark[2] that changes in capillary blood flow were due to opening and closing of the "precapillary sphincter," the last point distally where the endothelium is surrounded by vascular smooth muscle. This arrangement is assumed to occur in human capillaries. Previous reports have described the vasomotor activity of the conjunctival peripheral vasculature as irregular in rate, in degree, and in the duration of the observed phases of constriction and dilatation of the blood vessels.

Observations on conjunctival blood vessels in hypertension were made by Rudemann,[3] who, in 1933, noted progressive ischemia of the capillary bed with increasingly severe grades of hypertension. He also considered the excessive vascular tortuosity noted in these patients' conjunctivae to be a pathologic feature.

Lee and Holze,[4] in 1950, described the topographical and functional arrangements of conjunctival blood vessels in young normotensive adults as comparable to the findings in the rat omental vessels. They made measurements of corpuscular flow rate in arterioles, capillaries, and veins, and determined the threshold

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concentration of topical Adrenalin at which capillary blood flow ceased. The range of values for this method was between 1/20,000 and 1/50,000. The following year these authors reported their investigations on the conjunctival vessels in 45 patients with essential hypertension.[5] The authors concluded that no single feature observed could be described as characteristic, but when the patients were considered as a group, the "hypertensive pattern" included excessive tortuosity of the smallest blood vessels, narrowing of arterioles, augmented spontaneous vasomotor activity, and an increased sensitivity of the terminal vasculature to topical Adrenalin as compared with the findings in the previously reported normotensive patients. The capillary blood flow rates were slower than those of their normotensive group. Somewhat similar findings were reported also in cases of Cushing's disease, and pheochromocytoma.[6]

Landesman's group[7] made careful studies of large numbers of patients suffering from toxemia of pregnancy and eclampsia. The conjunctival blood vessels in these conditions showed increasing functional changes with the severity of the clinical state, and reached their highest expression in eclampsia, during which vascular caliber was small, arterioles were sometimes not detectable on account of continuous intense spasm, and the capillary bed was so ischemic as to be almost bloodless. The conjunctivae of 3 cases of toxemia were examined before and after the administration of Apresoline, without observable change.

The present study is an investigation of a method for the semiquantitative expression of vasomotor activity, and of the factors regulating human vasomotor phenomena. In addition, functional changes in the conjunctival blood vessels of hypertensive patients are described, both before and after ganglionic blockade.

METHODS

Observations were made on subjects in the sitting posture in a warm, darkened room, using a Zeiss Opton binocular microscope and slit-lamp illumination. After examination of the nasal and temporal quadrants of each eye, suitable areas were selected for further study by following an arteriole to its distal ramifications. At least four observations were made on each patient, and by means of sketches and photographs certain vascular patterns were re-examined on successive occasions, extending in some cases over many months. With practice, it became possible

TABLE I. AGE AND SEX DISTRIBUTION OF 50 NORMOTENSIVE AND 53 HYPERTENSIVE PATIENTS

PATIENTS	AGE						TOTAL
	10-19	20-29	30-39	40-49	50-59	60-69	
Normotensive							
Male	–	1	2	5	7	5	50
Female	1	1	2	6	10	10	
Untreated Hypertensive							
Male	–	1	2	7	7	5	53
Female	1	1	2	6	11	10	

in this way to locate any previously studied vascular unit with a high degree of certainty. When observing vasomotor activity, the blood pressure was recorded as closely as possible to the time of the observations.

Photographs were taken by a Leica camera fitted to one arm of the binocular microscope, on either standard film or Kodachrome, using a synchronized electronic flashgun for lighting.

Fifty-three cases of untreated hypertension were studied, the diagnosis of hypertension resting on the clinical findings of repeated casual arterial blood pressure readings of 150/100 mm. Hg (usually much higher), with or without evidence of hypertensive heart disease (Table I). Forty-four patients in the series showed hypertensive fundal changes, Grades 2 to 4 according to the grading of Keith, Wagener and Barker.[8]

A control group of 50 normotensive patients similar to the hypertensive series in age grouping and sex distribution was studied (Table I). These normotensive patients were attending the hospital service for a variety of reasons unrelated to hypertensive, cardiovascular, or hemopoietic disorders. Diabetic patients were excluded. Additionally, 30 asymptomatic subjects, 20 to 30 years of age, were examined.

During tests with parenteral hexamethonium, an assistant introduced the needle and took observations of the blood pressure, waiting 3 minutes after venipuncture had been performed before administering from 12 to 15 milligrams of the drug.

RESULTS

1. *Vasomotor Activity and the "Vasomotor Rate."*—In all patients, both normotensive and hypertensive, spontaneous vasomotor activity was observed resulting in an intermittent peripheral blood flow. In terminal arterioles, vasomotor activity was evident as a type of peristaltic vascular contraction. As this wave passed distally, it created a short break in the observed arterial blood column, ahead of which break the arteriolar wall seemed to dilate, as did the smallest terminal vessels when the vasomotor wave approached (Figs. 1 and 2).

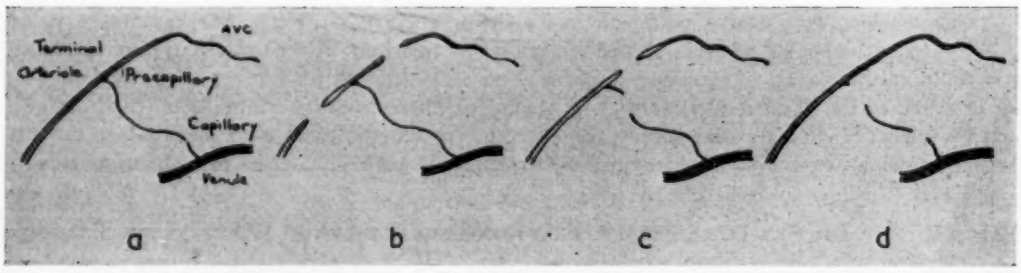

Fig. 1.—Intermittent blood flow in capillaries and arterioles resulting from vasomotor activity. In *a* there is continuous flow, while in *b* there is intermittent arteriolar blood flow. Intermittency of blood flow, in both arteriole and capillary, is shown in *c*, while *d* shows only precapillary vasomotor activity.

This type of vasomotor activity was present in only half the normotensive subjects, but was invariably present in the hypertensive patients. In the capillaries and arteriovenous communications (not true arteriovenous anastomoses[9]) vasomotion resulted in intermittent blood flow through these terminal vessels.

Periods of active capillary blood flow, of variable length, were observed to alternate with equally variable phases of complete capillary shut down, as previously described.[4,5] It is this variability in occurrence and duration of vas-

omotor activity which has led to previous descriptions of vasomotor phenomena as being "totally irregular."

It is emphasized in the present study that even during a phase of active capillary blood flow, the capillary blood columns are discontinuous (Figs. 1 and 2). The cellular blood columns, of variable length, are interrupted by clear spaces which, originating at the precapillary sphincter, pass distally along the capillary until a collecting venule is entered. Here vasomotor activity ceases.

Interruptions in the capillary blood column were noted to arise in two ways: (1) by the arrival at the precapillary sphincter of a break in the arteriolar blood column as the vasomotor wave passes distally, and (2) by breaks in the capillary blood column which were observed to originate at the precapillary sphincter in the absence of any recognizable vasomotor activity in the parent arteriole.

In the present study such breaks in the blood columns were observed and counted as they flowed past some selected point in the proximal end of a capillary (or terminal arteriole). The number of interruptions per minute in the blood column is called the vasomotor rate.

In spite of the previously mentioned lack of metrical regularity of recurrence and duration of vasomotor activity, it was found that there was a closely comparable vasomotor rate (as defined above) in similar functional units throughout the conjunctiva at different examinations on any one patient. The values for the vasomotor rate per minute showed great individual variation. However, the value in the identical functional unit in any patient with a stable blood pressure was found to be remarkably constant for that person—e.g., 14 ± 2 interruptions per minute—in observations extending in some instances over a period of a year or more.

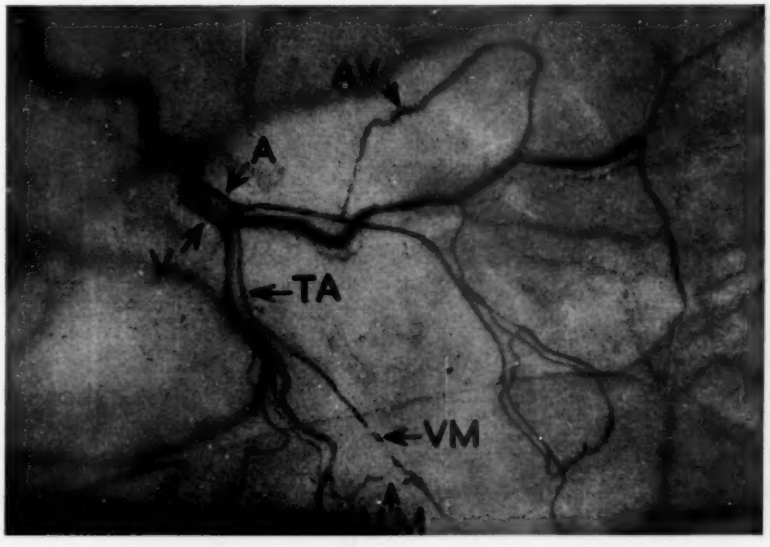

Fig. 2.—Normotensive conjunctival capillary bed, showing all the constituent blood vessels. Note the vasomotor interruptions of the capillary blood column, as well as similar interruptions in the corresponding AV ("thoroughfare") channel.

The vasomotor rate in hypertensive and normotensive populations: When the frequency distribution of vasomotor rates in the hypertensive and normotensive populations was compared, a highly significant difference became apparent (Fig. 3).

The peak of the distribution curve of vasomotor rates among the normotensive patients fell at the rate of 20 per minute, while that of the hypertensive patients fell at the rate of 35 per minute. Of the normotensive patients, only 4

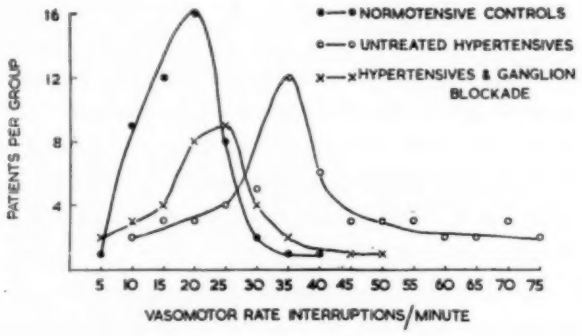

Fig. 3.—Distribution curves of vasomotor rates in normotensive controls, untreated hypertensives and hypertensives treated with ganglionic blocking drugs. The vasomotor rate is expressed as the number of interruptions of the blood column per minute, as observed in a minute conjunctival blood vessel

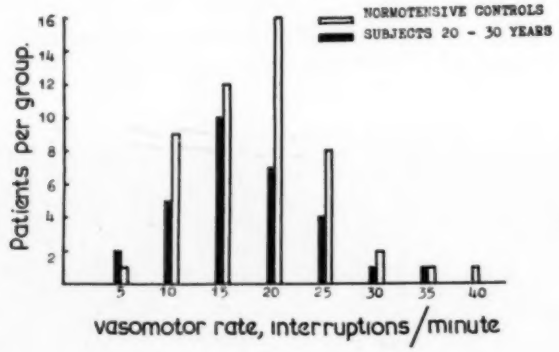

Fig. 4.—Distribution of vasomotor rates in normal subjects between 20 and 30 years of age, and in normotensive patients used as controls, who were mostly over 40 years of age. The vasomotor rate is expressed as the number of interruptions of the blood column per minute, as observed in a minute conjunctival blood vessel.

per cent were found to have vasomotor rates greater than 34 per minute, while in 68 per cent of the hypertensive patients the vasomotor rate exceeded 34 per minute.

In studying the effect of age upon the vasomotor rate, a comparison was made between the normotensive control group (86 per cent of whom were between 40 and 70 years of age) and 30 healthy subjects who were between 20 and 30 years of age (Fig. 4). The peak of the distribution curve of vasomotor rates for the group of older patients falls at a rate of 20 per minute, and the peak for

the group of younger patients falls at a rate of 15 per minute. The difference, however, is not statistically significant (Fig. 4; $X^2 = 1.31$, 3 d.f.). The number of young hypertensive patients was inadequate to test the possibility of age influencing the vasomotor rates of the hypertensive series. The vasomotor rate was not influenced by the sex of the patients examined in either the hypertensive or normotensive groups.

Factors influencing the vasomotor rate: In all patients tested, both normotensive and hypertensive, it was possible to lower the vasomotor rate by means of ganglionic blockade (Figs. 3 and 5). In normotensive subjects with an initial low vasomotor rate, ganglionic blockade on occasions almost abolished recogniz-

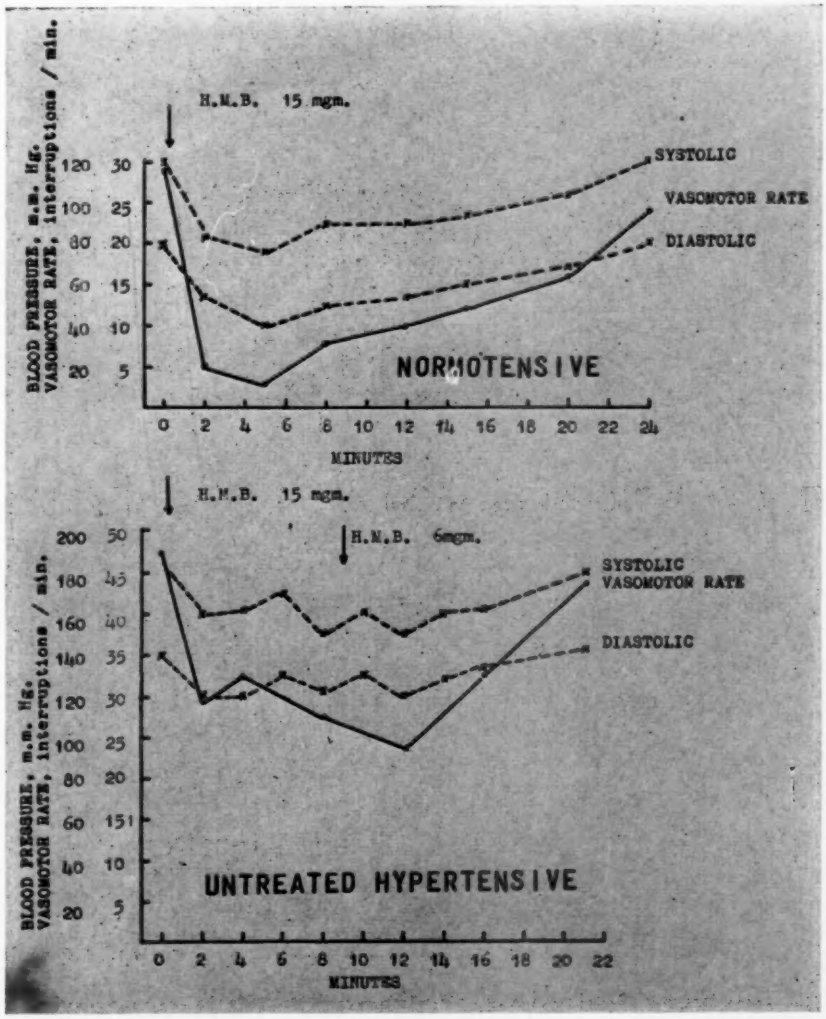

Fig. 5.—Effect of intravenous hexamethonium on the blood pressure (dashed line) and on the vasomotor rate (solid line) in a normotensive and in a hypertensive subject. The vasomotor rate is expressed as the number of interruptions of the blood column per minute, as observed in a minute conjunctival blood vessel.

able vasomotor activity. In untreated hypertensive patients such an effect could also be produced, but was avoided since it necessitated lowering the arterial pressure to a potentially dangerous degree.

One patient with severe spontaneous postural hypotension and diabetic neuritis exhibited an identical fall in vasomotor rate as her blood pressure dropped toward syncopal levels, as did normotensive patients under substantial ganglionic blockade. At a systolic blood pressure of 60 mm. Hg, conjunctival vasomotor activity ceased, and there was very slow peripheral blood flow.

Stellate ganglionic block by local Xylocaine anesthesia was performed on 2 hypertensive patients and on 1 normotensive patient. The initial vasomotor rates were 40 and 34 in the hypertensive patients and 16 in the normotensive patient. Following stellate ganglionic block, vasomotor activity was totally abolished and the vascular beds became plethoric.

In patients in whom anxiety was accompanied by a very labile blood pressure, the vasomotor rate was correspondingly variable, e.g., 46 units per minute at 230/150 mm. Hg, and 22 units per minute at 150/100 mm. Hg, without drug influence. Anxiety unaccompanied by a labile blood pressure did not have any influence on vasomotor rates.

2. *Some Functional Changes in the Hypertensive Conjunctival Capillary Bed.*—No specific feature, either anatomical or functional, was found by which a diagnosis of hypertension might be made from conjunctival microscopy alone, although one or more abnormalities occurred in approximately 80 per cent of the untreated hypertensive patients.

The majority of the patients in the untreated hypertensive group were found to have vasomotor rates in excess of the normotensive control patients (Fig. 3). Although as a group the vasomotor rates of the hypertensive patients were faster than those of the normotensive population, there was no special significance of the rate in any individual patient. Thus, hypertensive patients with low vasomotor rates often had clinical evidence of severe hypertensive heart disease. Conversely, a very high vasomotor rate did not necessarily imply a more severe degree of hypertension, although all 6 cases of malignant hypertension had vasomotor rates exceeding 40 per minute.

Increased spontaneous vasomotor activity was also demonstrated by the observation of spasm in the conjunctival terminal arterioles of untreated hypertensive subjects. Arteriolar spasm, while often associated with a high vasomotor rate was found to be present in substantial degree in some untreated hypertensive patients with low vasomotor rates. Areas of nonpropagated spasm were observed, rendering short segments of terminal arterioles bloodless for intervals of from a few seconds up to a minute. Total spasm of an entire arteriole, previously reported in eclampsia,[7] was encountered in one case of malignant hypertension (Fig. 10,*A*). Prior to treatment, this arteriole showed no evidence of blood flow on repeated examinations.

Severe vascular spasm resulted in an ischemic capillary bed, further accentuated by a preponderance of "closed" over "open" phases of capillary blood flow. Gross conjunctival capillary ischemia is shown in Fig. 6, together with waves of vasomotor activity in an arteriole, and severe (renal) anemia.

The threshold concentrations of dilute topical Adrenalin solutions required to arrest capillary blood flow were measured in the untreated hypertensive group, in the normotensive control series, and in 30 healthy subjects aged 20 to 30 years. The method of Lee and Holze[4] was employed, with closely similar results (Fig. 8). The range of threshold concentrations of Adrenalin in the normotensive controls lay between 1/10,000 and 1/200,000, and in the untreated hypertensive patients

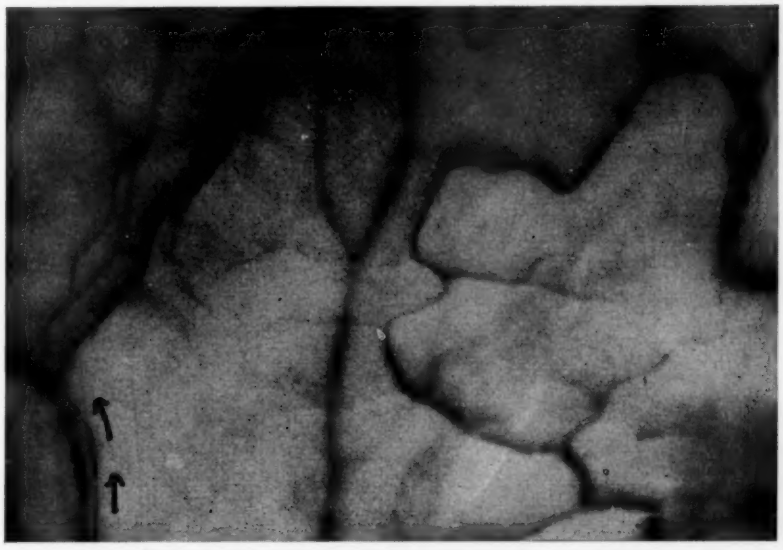

Fig. 6.—Illustration of the occurrence of waves of peristaltic vasomotor activity in an arteriole. The direction of movement is shown by the arrows. Generalized capillary ischemia is seen to the right of the arrows, due to arteriolar spasm.

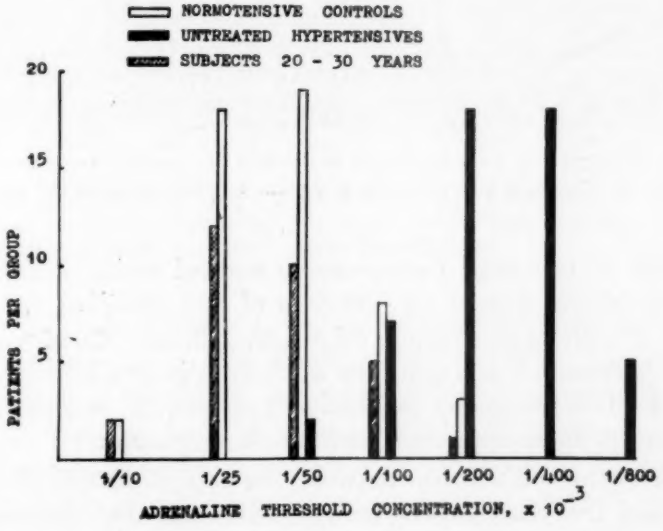

Fig. 7.—Distribution of the threshold concentrations of Adrenalin capable of obliterating the minute vessels of the conjunctiva. It will be seen that higher dilutions are effective in hypertensive patients, and stronger solutions are required in normotensive subjects.

the range was between concentrations of 1/50,000 and 1/800,000. There was a highly significant difference of threshold level between the hypertensive and normotensive populations; 75 per cent of the normotensive controls responded to threshold concentrations of 1/25,000 or 1/50,000, whereas 70 per cent of the hypertensive series responded to threshold concentrations of 1/200,000 or 1/400,000.

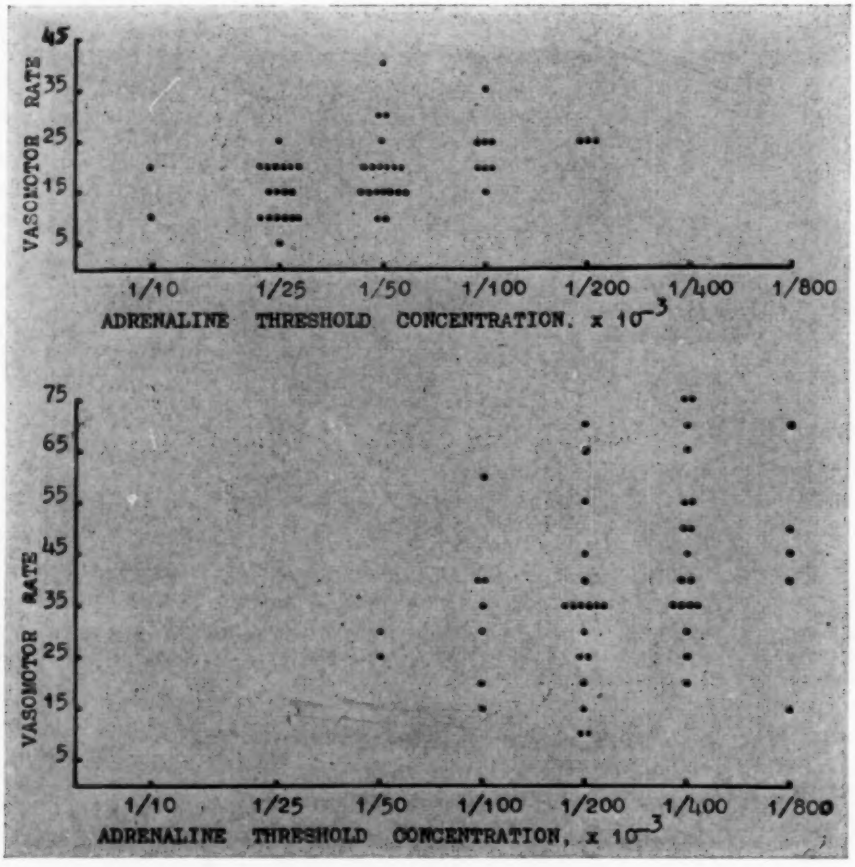

Fig. 8.—Each dot represents the relationship in one and the same patient between the vasomotor rate per minute and the threshold concentration of Adrenalin which arrested the capillary circulation.

Comparison of the total normotensive control series with the 30 young normotensive subjects showed no influence of age grouping on the threshold concentrations of Adrenalin (Fig. 7; $X^2 = .33$, 2 d.f.). There was no influence of sex on the threshold concentrations of Adrenalin in either hypertensive or normotensive control groups (hypertensive patients, $X^2 = 1.62$, 2 d.f.; normotensive distribution identical in male and female members).

Fig. 8 shows the relationship between the topical threshold concentrations of Adrenalin and the vasomotor rates in patients of the normotensive control group and the untreated hypertensive group. There is an association in both series between the occurrence of high vasomotor rates and high sensitivity to topical Adrenalin solutions in individual patients.

3. *Effects of Ganglionic Blockade on Hypertensive and Normotensive Conjunctival Blood Vessels.*—Observations were made on the effect of intravenous hexamethonium bromide on the conjuctival blood vessels in 10 normotensive and 15 untreated hypertensive patients. Twenty-four untreated hypertensive patients from the series of 53 were followed at intervals until stabilized on an effective regimen of oral pentolinium or oral mecamylamine. Five of these 24 patients were tested also with intravenous methonium before starting therapy. No reversal of anatomic hypertensive changes was apparent in treated patients followed for 3 months or more.

As previously described, both normotensive and hypertensive patients demonstrated varying degrees of depression of the vasomotor rate under ganglionic blockade. The fall in vasomotor rate following oral therapy with pentolinium or mecamylamine corresponded to that induced by parenteral methonium

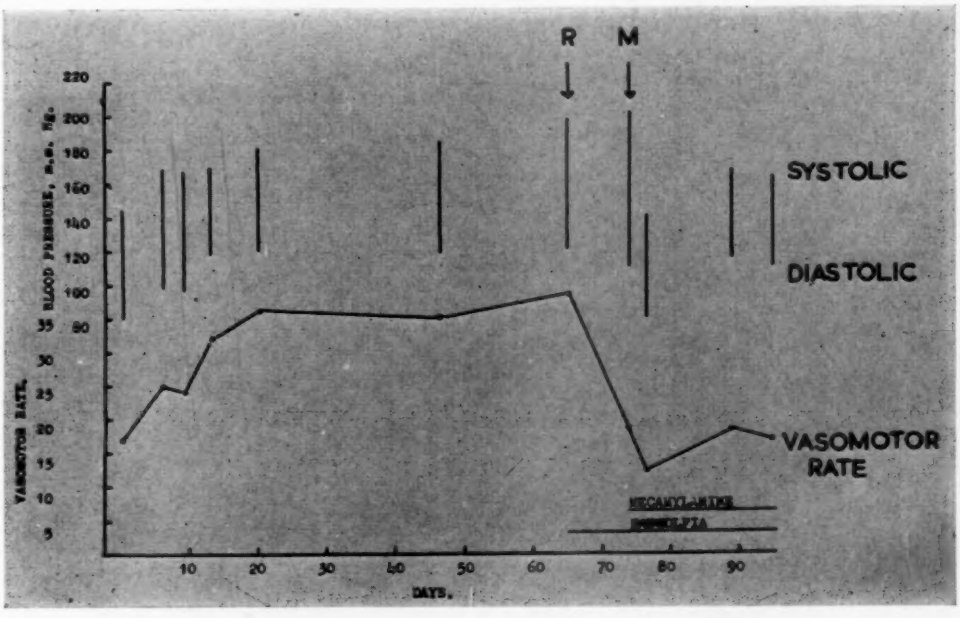

Fig. 9.—Rise in blood pressure (vertical lines) and vasomotor rate (line with dots) during recovery from infarction in a male hypertensive patient. A fall of blood pressure and of vasomotor rate is seen after the administration of rauwolfia alkaloid and mecamylamine.

in those patients previously tested. As patients became stabilized on a regimen of ganglionic blocking drug, the vasomotor rate became stabilized at a lower level, but remained in nearly all cases more labile than in the untreated state, fluctuating with changing levels of drug activity. Fig. 3 shows the distribution of vasomotor rates in 34 patients under ganglionic blockade, as the means of the minimum rates observed. Patients followed for some months beyond the initial period of stabilization on an effective regimen of oral pentolinium or mecamylamine often showed a further fall in vasomotor rate without alteration in their blood pressure readings.

Fig. 9 shows changes in vasomotor rate in a 56-year-old male hypertensive patient who had suffered a cardiac infarction, from which he was convalescing at the time observations began. There was a steady rise in vasomotor rate as his blood pressure slowly returned toward its preinfarction hypertensive levels, until the institution of rauwolfia alkaloid (little change of blood pressure but rapid fall in vasomotor rate) and, finally, a combination of rauwolfia and mecamylamine as definitive therapy.

In hypertensive patients, ganglionic blockade often caused marked increase in the diameter of the arteriolar blood columns (Fig. 10,*B*), especially where

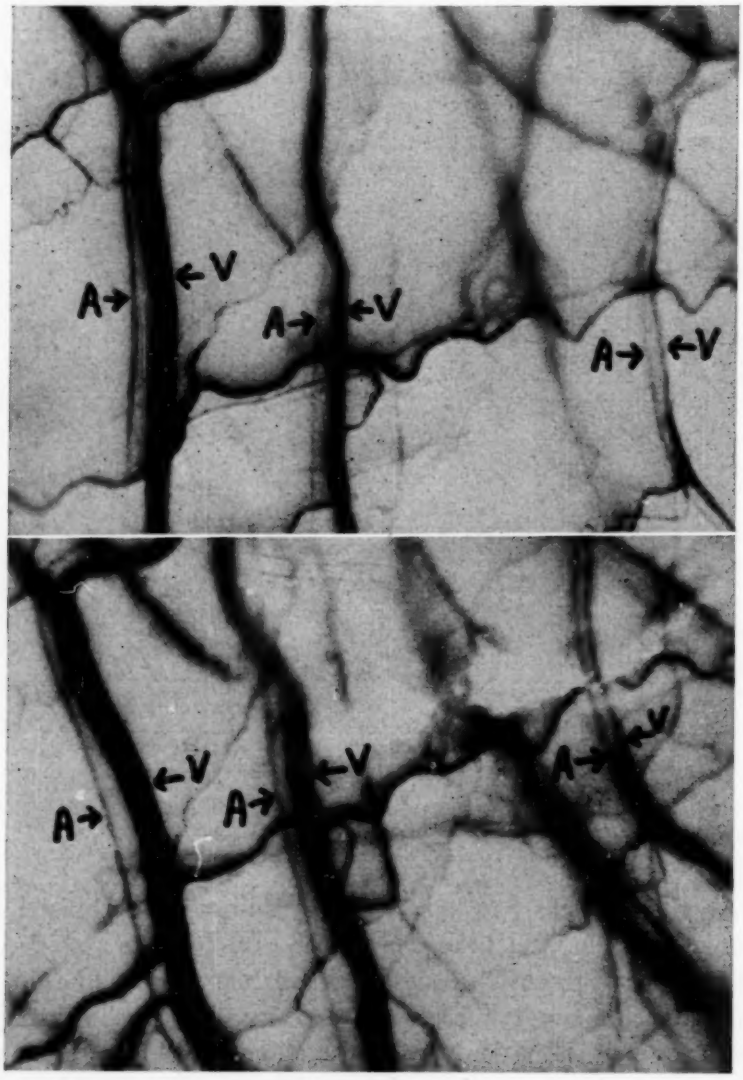

Fig. 10.—*A*, Conjunctival vessels of hypertensive patient showing arteriolar spasm and capillary ischemia. (A is an artery; V is a vein.) The positions marked with arrows correspond approximately in parts *A* and *B* of this illustration. *B*, Conjunctival vessels of same patient after administration of ganglionic blocking drugs, showing enlargement of veins and venous capillaries. An increase in the number of visible capillary blood vessels is apparent.

spasm had been prominent previously. Change in normotensive arterial caliber, on the other hand, was slight or absent.

There was a definite decrease in arteriolar spasm in all hypertensive patients in whom ganglionic blockade restored blood pressure readings to normal. With lessening of spasm, an increase in capillary blood flow rate was readily apparent, although it was not measured.

Venous plethora was the most striking change noted on low-power observation of the conjunctival vessels of all normotensive patients and the majority of hypertensive patients subjected to ganglionic blockade (Fig. 10, *A* and *B*). The capillary bed, on the other hand, often remained ischemic in appearance, despite venous plethora. The venular blood columns developed a "granular" appearance in many instances during ganglionic blockade (Fig. 6).

There was no change in the raised sensitivity of the hypertensive conjunctival capillary bed to topical solutions of Adrenalin in 20 patients tested before and after stabilization on oral pentolinium or mecamylamine, and similarly in 3 patients during parenteral methonium blockade.

DISCUSSION

Observations on vasomotor phenomena in the human conjunctival vascular bed agree with previous reports on normotensive and hypertensive patients. To these views has been added a method of counting the interruptions per minute occurring in the capillary or arteriolar blood columns as a result of vasomotor activity, in an attempt to derive some quantitative expression of vasomotion.

Despite the complete lack of any pattern of metrical recurrence of the vasomotor phenomena, the constant level of the vasomotor rate over long periods, when determined in the same functioning unit in any patient with a stable blood pressure, was most impressive.

While vasomotor activity is an intrinsic feature of the peripheral vascular smooth muscle, the relation of this phenomenon in the human conjunctival capillary bed to the functional activity of the sympathetic nervous system seems quite clear. The relationship between the vasomotor rate and rising blood pressure (Fig. 10), and the changes in vasomotor activity with ganglionic blockade or spontaneous postural hypotension, stellate ganglionic block, and anxiety all support this view. It is possible that variations in the proportions of neurogenic and non-neurogenic components of blood pressure homeostasis may account for individual differences of vasomotor activity within the normotensive population.

There was a marked difference in the frequency distribution of vasomotor rates between the normotensive and untreated hypertensive populations. Since human vasomotor activity is influenced by the sympathetic nervous system, the occurrence of high vasomotor rates in hypertension agrees with evidence that in this condition there is an increase in the neurogenically maintained part of the blood pressure (Doyle and Smirk[10]).

In this connection it is of interest that 8 out of the 12 hypertensive patients with lowest vasomotor rates (less than 30 per minute) were suffering from left or general heart failure. This observation may be related to the finding by Kilpatrick[11] that, in heart failure, the supplemental blood pressure (casual minus

basal blood pressure), which is mainly of neurogenic origin, forms a smaller proportion of the casual blood pressure than in control subjects.

In man, Alam and Smirk[12] demonstrated an increased reactivity to pressor stimuli, and Doyle and Black[13] observed an increased response above the normal to pressor drugs in patients with essential hypertension, especially after homeostatic controls had been restrained by the administration of ganglionic blocking drugs. McQueen and co-workers[14,15] found enhanced vascular reactivity in rats with renal and renoprival hypertension, as compared with normal controls. Smirk[16,17] regards increased vascular reactivity as one of the components in the pathogenesis of essential hypertension. Observations reported in this paper show that in hypertension the arrest of conjunctival capillary blood flow can be effected by more dilute solutions of Adrenalin than in normotension. In normotensive subjects, increasing age does not appear to exert any significant effect on the reactivity of the conjunctival capillaries to topically administered Adrenalin. The difference in vascular reactivity is, therefore, more likely to be related to the hypertensive state than to changes which take place with age.

The decrease in spontaneous vasomotor activity of both normotensive and hypertensive patients, together with venous plethora, constituted the most striking features resulting from the action of ganglionic blocking drugs. In countering the arteriolar spasm of hypertension such drugs resulted not only in an increase of arterial caliber but also in a decrease in the frequency and magnitude of the "constricted" phases resulting from excessive spontaneous vasomotor activity.

SUMMARY

1. Spontaneous vasomotor activity of the human conjunctival capillary bed is described, and an attempt is made to derive a quantitative expression of vasomotor activity—the vasomotor rate—in normotensive and hypertensive populations.

2. The influence of methonium, spontaneous postural hypotension, stellate ganglionic block, and anxiety upon vasomotor activity in the conjunctival blood vessels is described.

3. Hypertensive patients demonstrated excessive spontaneous vasomotor activity, arteriolar spasm, and ischemia of the conjunctival capillary bed, together with increased sensitivity of the hypertensive conjunctival blood vessels to topical Adrenalin solutions.

4. In both normotensive and hypertensive patients there was a tendency for those patients with high sensitivity of the conjunctival capillaries to topical Adrenalin to show correspondingly high values for their vasomotor rates.

5. In both normotensive and hypertensive patients ganglionic blockade induced a fall in the level of spontaneous vasomotor activity, together with the occurrence of venous plethora.

6. In countering the arteriolar spasm of hypertension, ganglionic blockade decreased the frequency and magnitude of the "constricted" phases, and increased arteriolar caliber. Normotensive arteriolar caliber was unchanged.

7. There was no change in the conjunctival capillary sensitivity to topical Adrenalin in patients under ganglionic blockade.

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The Effect on Atrial Impulse Formation of a Hypertonic Solution of Sodium Chloride Applied Focally

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It is a well-known fact that faradic stimulation of one of the vagus nerves in the neck of a dog may lead occasionally to the sudden appearance of atrial flutter or fibrillation. This observation has been made incidentally by several authors and has been discussed by others.[5,11,13,16,22] However, this occurrence can never be predicted. It is also known that if acetylcholine and physostigmine do not cause atrial fibrillation by themselves, the addition of electrical vagus stimulation will cause the occurrence of this arrhythmia.

We found that it is possible to obtain atrial flutter or fibrillation with great regularity if a highly concentrated solution of sodium chloride is injected subepicardially into the sinus node area of the right atrium and the vagus nerve is stimulated.

METHOD

Mongrel dogs, weighing on the average 10 kilograms, were anesthetized with morphine and Nembutal, administered intraperitoneally. The heart was exposed after artificial respiration had been established. The vagus nerves were cut in the neck, and a shielded electrode was applied to the right vagus nerve. The electrocardiogram was registered in Lead II. A solution of 20 per cent sodium chloride in water was injected subepicardially over the area of the sinus node (taenia terminalis) and a small bleb formed. The procedure is more easily done in this location than in any other part of the atria because of the thickness of the epicardium and the layer of connective tissue beneath it. The quantity injected amounted to about 0.05 c.c. Faradic stimulation of the vagus was performed with the aid of a Cambridge Inductorium about 30 seconds after the injection.

RESULTS

Atrial fibrillation with or without short periods of flutter appeared in all of 23 experiments. In most experiments the attacks could be provoked repeatedly—in fact, up to six times. In 4 experiments they appeared only after

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a second injection of sodium chloride. In all experiments the vagi were stimulated three times for 10 seconds each before the injection, in order to find out whether atrial fibrillation would appear without the injection. Atrial fibrillation without injection occurred only once in 1 experiment and was not reproducible.

The time of appearance of the fibrillation varied. Sometimes it was immediate, as in Fig. 3,*A*, while in other experiments it was present only after a stimulation lasting 10 seconds. The fibrillation lasted less than 1 second in some attempts and up to 110 seconds in others. In 2 experiments atrial fibrillation followed the injection without the vagus stimulation. Atrial extrasystoles often appeared after the injection (Figs. 1,*A* and 3,*D*) or after vagus stimulation but were suppressed during the vagus stimulation (Fig. 3,*D*). Stimulation of the right or left vagus was equally effective.

The fibrillation usually appeared, as in Figs. 1,*A*, 2,*A* and 3,*A*, just following the QRS complex. Of 57 attacks of fibrillation which developed under these conditions, in only three instances did the attack start, as in Fig. 3,*B*, independently of a ventricular beat, and in two of these there were only a few rudimentary fibrillatory waves. Fig. 3,*B* is the only instance of prolonged fibrillation arising during diastole. Usually the flutter or fibrillation waves were visible between the QRS and T waves of a conducted or escaped beat, and in most cases there were a few slower flutter waves which quickly changed into fibrillation.

In 2 experiments a paroxysmal atrial tachycardia appeared. The atrial rate was 250 beats per minute in one experiment (Fig. 4) and 236 in another. These attacks of paroxysmal atrial tachycardia could be recognized by the paroxysmal appearance of premature, abnormal P waves, and by the fact that vagus stimulation did not lead to an increase of atrial rate as in flutter, but to a sudden abrupt end of the tachycardia (Fig. 4,*A* and *C*).

Vagus stimulation during flutter or fibrillation always elicited the phenomenon of re-excitation, and fine fibrillation appeared with very high rates of the fibrillation waves (Figs. 1,*C* and 2,*C* and *D*).

We attempted to employ lower concentrations of sodium chloride, that is, a 5 and a 10 per cent solution. Fibrillation appeared with these solutions but not with the same regularity and high incidence as with a 20 per cent solution.

In 2 experiments with atrial flutter and in 3 with atrial fibrillation elicited by the method described above, the arrhythmia lasted long enough so that a ligature could be applied across the taenia terminalis, thus interrupting conduction in this structure and the adjacent areas, about 1 cm. to the right and left. In no instance did the form of the flutter or fibrillation waves change when the ligature was tightened, and in no instance was the arrhythmia stopped by this procedure (Fig. 3,*C*).

DISCUSSION

While the effect of the variation in concentration of potassium and calcium in the extracellular fluid on the polarization and depolarization process of myocardial cells has been extensively studied, little work has been done on the effect of variations in concentration of sodium. One of the reasons for this is the fact

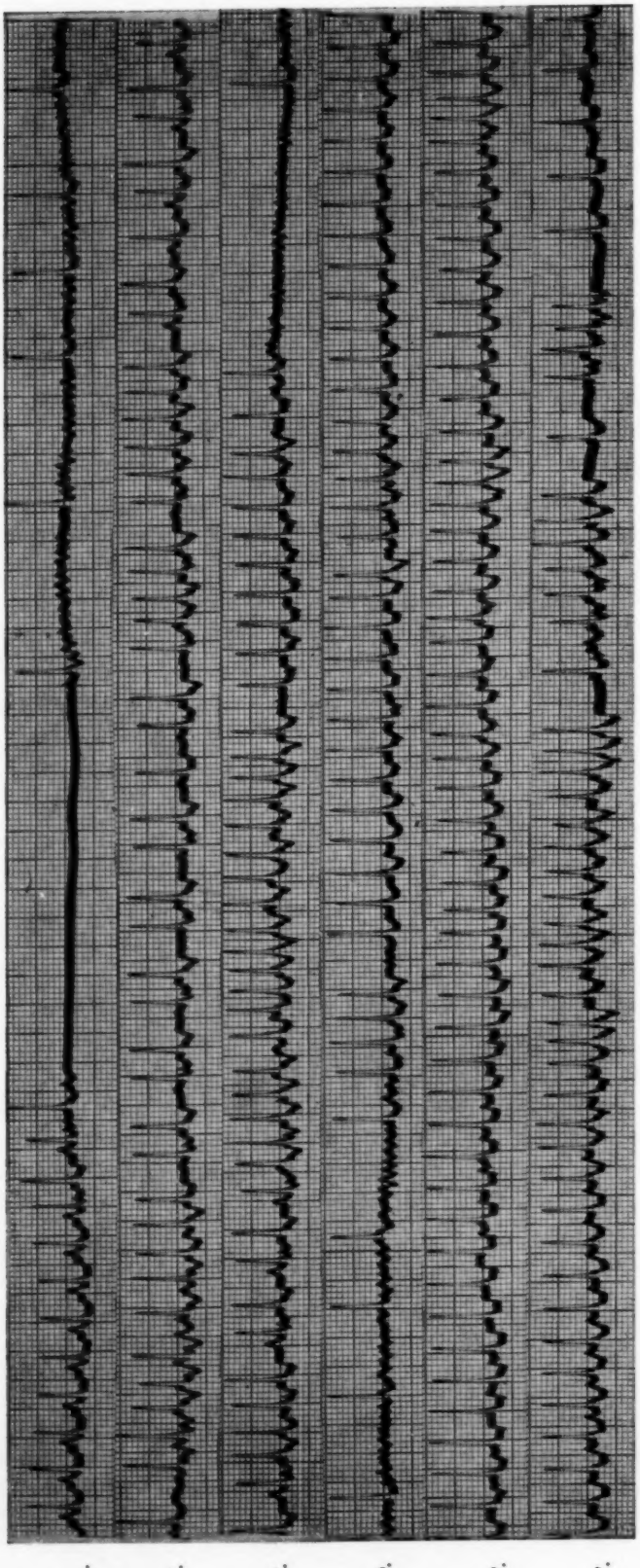

Fig. 1.—Experiment of October 15. Vagal stimulation starts (*A*) just after the appearance of several atrial extrasystoles. A long cardiac standstill follows, but immediately after an escaped atrial beat, atrial fibrillation sets in. It stops spontaneously in *B* and is followed by an atrial bigeminal rhythm and a series of atrial extrasystoles. Fibrillation begins again spontaneously in *C*; the right vagus nerve is stimulated (end of *C* and beginning of *D*). The fibrillation changes into flutter in *D*, and a series of atrial extrasystoles appear in *F* just before sinus rhythm reappears. The six strips are continuous.

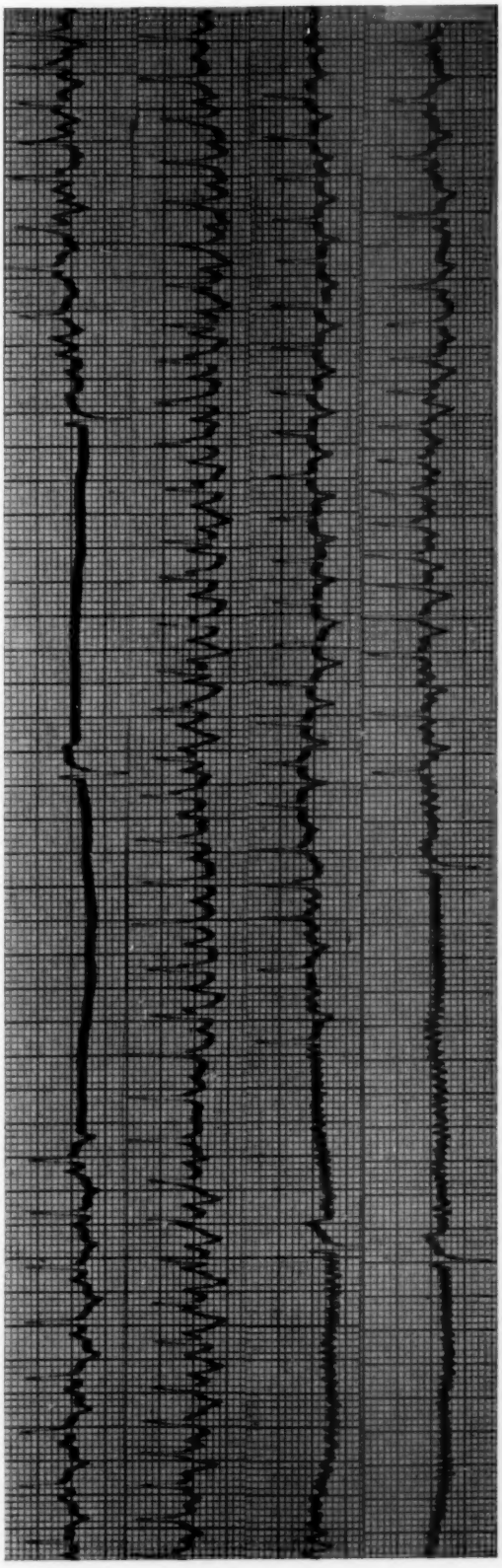

Fig. 2.—Experiment of May 14. Vagal stimulation following the subepicardial injection of the solution of sodium chloride causes cardiac standstill with two escaped ventricular beats (*A*). In the first of these two beats an atrial extrasystole can be seen between the QRS and the T waves. The second escaped beat is followed immediately by atrial fibrillation. In *B* the fibrillation changes spontaneously to flutter. Vagus stimulation is repeated twice (*C* and *D*) and changes the flutter instantly into fibrillation. Sinus rhythm appears at the end of *D*. These strips are continuous.

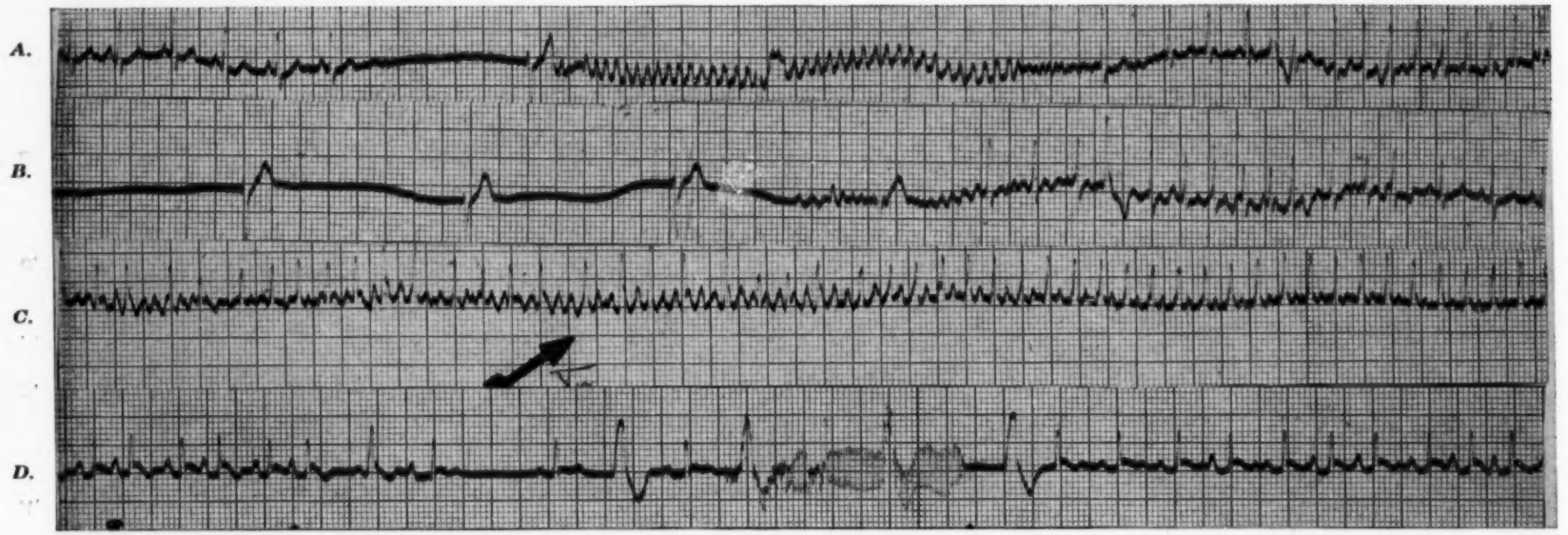

Fig. 3.—*A* was obtained in an experiment on May 7. It shows the beginning of atrial flutter which spontaneously changes into fibrillation during vagus stimulation. The flutter starts typically immediately after a ventricular beat. In the second strip (*B*), obtained in the same experiment a few minutes later, vagus stimulation leads to a series of slow escaped ventricular beats. A short attack of atrial fibrillation sets in during diastole after the third escaped beat of *B*. Three sinus beats appear at the end of the tracing. Here, as in the other tracings, the end of vagal stimulation is recognizable by the sudden increase in ventricular rate. In the experiment of June 6 (*C*), atrial fibrillation and flutter appear after vagus stimulation following the injection of sodium chloride. During the arrhythmia a ligature is placed across the taenia terminalis, interrupting conduction in this structure and the adjacent areas about 1 cm. to the right and left of it. In spite of the interruption of the conduction of this pathway the flutter remains unchanged. In *D*, obtained on February 12, an atrial bigeminy has followed the injection of sodium chloride. During vagus stimulation the atrial extrasystoles disappear, and reappear shortly after. Ventricular extrasystoles are seen during the stimulation.

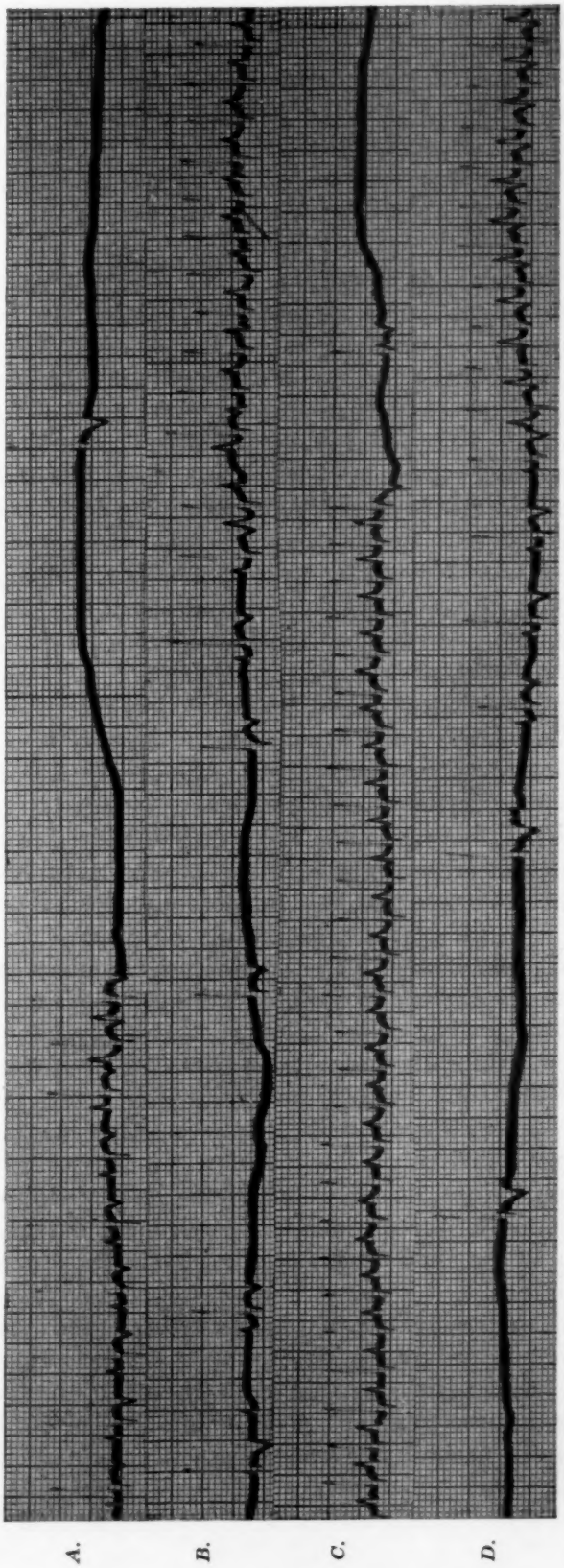

Fig. 4.—In the experiment of April 23, a paroxysmal atrial tachycardia appears spontaneously following the subepicardial injection of sodium chloride (*A*). Vagus stimulation which starts after the second beat of the tachycardia causes prolonged cardiac standstill interrupted by rare ventricular and sinus escape beats (*A* and *B*). After the end of the stimulation the paroxysmal atrial tachycardia starts again, but a renewal of the vagal stimulation stops it at once (*C*). The tachycardia reappears after the second stimulation is ended (*D*). The four strips are continuous.

that higher concentrations of sodium lead to strong osmotic effects and changes in pH. These factors certainly play a role in our experiments. However, 20 years of experience on ectopic impulse formation evoked by the topical application of substances has shown the arrhythmias to be due mainly to specific effects of the substances and not to general physical actions.[19,20] Application of solutions of concentrated glucose, acids, and other agents causing marked alterations of the tissue does not lead to the effects described in this report and in previous ones.

Changes in the concentration of sodium chloride do not have an appreciable influence on the resting potential of nerve cells.[8,9,21] This has also been confirmed for cardiac cells.[6] However, when hypertonic solutions of sodium chloride were used, an increase in the duration of the action potential was seen. A linear relation has been found between sodium concentration and the duration of ventricular action potential.[2] The rate of rise of the action potential is proportional to the external sodium concentration. The reversed potential difference across activated membranes is increased by solutions containing a higher concentration of sodium.[8,9]

We may assume that the gradient of the sodium ion is changed in our experiments by the application of concentrated solution of sodium chloride. It is possible that the entrance of sodium into the cell, initiating and causing its activation, is facilitated by this application.

Application of hypertonic solutions of sodium chloride to the surface of the atria or ventricles of the dog's heart leads to the temporary appearance of extrasystoles with fixed coupling or tachycardias.[15] Apparently an increased sodium concentration facilitates premature depolarization.

In this connection it is interesting to note that atrial fibrillation during vagus stimulation appeared with regularity when a 20 per cent solution of sodium chloride was used, whereas it was seen only occasionally with a 5 and 10 per cent solution; this result is in agreement with the observations of Langendorf[12] on the isolated (clamped) apex of the frog's ventricle. Langendorf observed up to 80 pulsations following application of sodium chloride crystals or on application of a saturated solution of sodium chloride, but no contractions appeared with less concentrated solutions. Substances applied to the cardiac surface are rapidly absorbed. It is possible therefore that higher sodium concentrates exert an effect for a longer time. Even with the use of the 20 per cent solution the phenomenon described in this paper lasted only a few minutes.

Vagus stimulation (or acetylcholine) facilitates the entrance of sodium into the cells[4]; the combination of the effects of acetylcholine and of sodium chloride in high concentration in the extracellular fluid leads to the appearance of fibrillation.

In connection with our experiments it is interesting to recall an observation on the classical nerve-muscle preparation.[14] Application of a crystal of sodium chloride on a nerve may lead to a tetanic contraction after one suprathreshold stimulus. It appears that the weak, subthreshold impulses caused by the sodium chloride become suprathreshold in the wake of a conducted impulse (Wedensky effect).

On the isolated frog heart the incidence of extrasystoles and ventricular fibrillation following ouabain was increased when higher concentrations of sodium chloride were used.[10] Ventricular fibrillation in the isolated rabbit heart, on the other hand, can be stopped by perfusion with a solution with low-sodium content.[7]

Of importance is the fact illustrated by the figures, that the fibrillation started in most instances shortly after a QRS complex of a ventricular escaped beat during the vagus stimulation. Often the fibrillation waves were visible before the T wave. One of the explanations readily at hand would be the increased vagal tonus which persists for a few hundredths of a second following a ventricular systole. However, since fibrillation or flutter waves were observed so early following ventricular activation, even after severing of both vagi in the neck, another mechanism must be responsible. We believe that a mechanical or electrotonic effect of ventricular systole (or depolarization) on the atria is possible, but improbable. It is possible that an ectopic atrial systole conducted to the ventricles during vagus stimulation initiates the flutter or fibrillation; thus, the connection between ventricular systole and the atrial arrhythmia is accidental. However, many of the ventricular beats during vagus stimulation are not preceded by P waves (Figs. 2,*A* and 3,*A*); they are escaped beats. Therefore, a relation between ventricular systole and the atrial arrhythmias must exist.

During vagus stimulation, introduction of one atrial stimulus shortly after the end of the refractory phase was followed by atrial fibrillation.[1] Multiple response to a single stimulus has been observed during vagus stimulation.[16]

The different response of two instances of atrial tachycardias to vagus stimulation should also be noted. While the electrocardiogram during the tachycardia (Fig. 4) does not differ apparently from that of flutter, vagus stimulation does not cause immediate fibrillation (re-excitation), but standstill. In other words, this tachycardia responded to vagus stimulation like a paroxysmal atrial tachycardia. The same could be observed in the tachycardias caused by the application of aconitine, in which the usual effect was also an increase of rate, although occasionally a tachycardia was stopped.[20] The reason for this difference in response can lie only in the finer mechanism of impulse formation and is unknown; however, such observations in connection with clinical observations force us to continue considering paroxysmal tachycardia and flutter as two different entities. While exceptions occur, flutter and paroxysmal tachycardia are seen in different types of patients. Flutter often changes into fibrillation spontaneously or under medication, whereas a paroxysmal atrial tachycardia does so only rarely. Many drugs valuable in paroxysmal tachycardias afford no help in flutter. Carotid pressure stops about 50 per cent of atrial tachycardias, while it never abolishes flutter.

The observation (Fig. 3,*C*) that a broad ligature across the sinus node area and the encompassing tissue to the right and left of the taenia terminalis does not interrupt or otherwise alter existing atrial flutter or fibrillation is important. In our opinion this precludes the possibility that these attacks are due to a circus wave traveling up or down the sinus node or around the intercaval bridge. This observation was made as early as 1928, with flutter caused by faradic stimulation of the atria[17] and, later, with aconitine-induced flutter.[18]

The abundance of sodium in our experiments enhances and creates ectopic impulse formation (atrial extrasystoles). This action is inhibited like the normal impulse formation during vagus stimulation. If, however, ectopic atrial beats occur during the vagus stimulation, any beat appearing during the vulnerable phase of a preceding one may lead to the repetitive firing and cause fibrillation.

CONCLUSIONS

Subepicardial injection of a 20 per cent solution of sodium chloride in the area of the sinus node (taenia terminalis) of the exposed heart of a dog in situ leads to the appearance of atrial extrasystoles.

Vagus stimulation elicits atrial flutter or fibrillation for a few minutes after the injection. While these arrhythmias were brief, they could be provoked with great regularity.

Flutter and fibrillation appeared in these experiments during a ventricular systole, that is, between the QRS complex and the T wave of an escaped beat during stimulation of the vagus.

The application of a broad ligature across the taenia terminalis and the adjacent area did not alter the existing flutter or fibrillation.

In 2 experiments atrial tachycardias appeared which were promptly stopped by vagus stimulation in the same manner as paroxysmal atrial tachycardias in patients.

The importance of these findings is evaluated.

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Ballistocardiogram During Paralysis With Succinylcholine

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Relative movement and reaction between the cardiovascular system and the internal body network and between the external body network and ballistocardiograph bed are important considerations in the theory of ballistocardiography.[1-7] Their significance in clinical ballistocardiography has been suggested by the work of Hakim and associates,[8] who demonstrated that wave forms similar to those found in the ballistocardiograms of patients with heart disease could be found in the records of normal subjects whose only indisposition was fatigue or muscular tension. An asynchrony in the heart and body linkage systems was proposed to account for the apparent abnormalities.

The subject of this report is the effect on the ultralow-frequency ballistocardiogram of complete abolition of muscular tone through paralysis with succinylcholine. The study was carried out both to evaluate the extent to which normal muscular tone affects the ballistocardiogram and to provide a control condition for the muscular relaxation of ether anesthesia.

METHODS

The characteristics and standardization of the ultralow-frequency ballistocardiograph patterned after the model of Reeves, Jones, and Hefner[9,10] have been described previously.[11] Coupling of the subject to the bed was enhanced through the use of shoulder straps. Lead II of the electrocardiogram, the carotid pressure pulse (Infraton pulse wave recorder), and the phonocardiogram were inscribed simultaneously with the ballistocardiogram on a Sanborn Poly-Viso recorder.

The subjects were three 19-year-old males who had fasted for 10 hours; these were the same men designated as Subjects I, II, and III in an earlier paper.[11] Each was permitted to rest on the bed until the recorded functions remained stable. Narcosis was then induced by intravenous injection of 250 to 500 mg. of thiopental sodium. About 4 minutes later a paralyzing dose of succinylcholine was given intravenously and supplemented by intermittent injections of the drug sufficient to maintain complete paralysis and apnea for 6 to 10 minutes; the mean total dose of succinylcholine was 47 mg. Aeration was maintained by intermittent positive pressure 100 per cent oxygen at a maximum mask pressure of 10 mm. Hg through a closed circle Heidbrink Kinet-O-Meter with soda lime absorbent. When ballistocardiograms were taken during paralysis, the mask was removed and the patient allowed to remain apneic for 5 seconds. Records during the control and recovery periods were taken with the subject in the mid-expiratory phase of respiration.

Amplitudes of the I and J waves were measured as deflections from the base line and referred to the heights of these waves during the control period for purposes of comparison.

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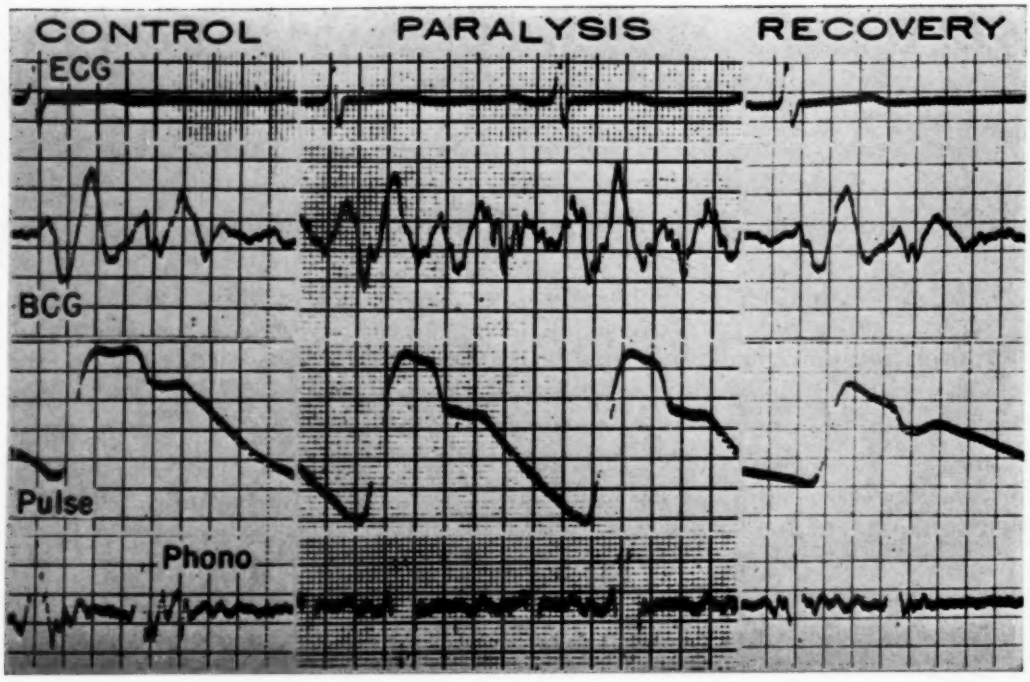

Fig. 1.—Electrocardiogram, ballistocardiogram, carotid pressure pulse, and phonocardiogram in Subject I during the control period, paralysis, and recovery. Paper speed, 50 mm./sec.

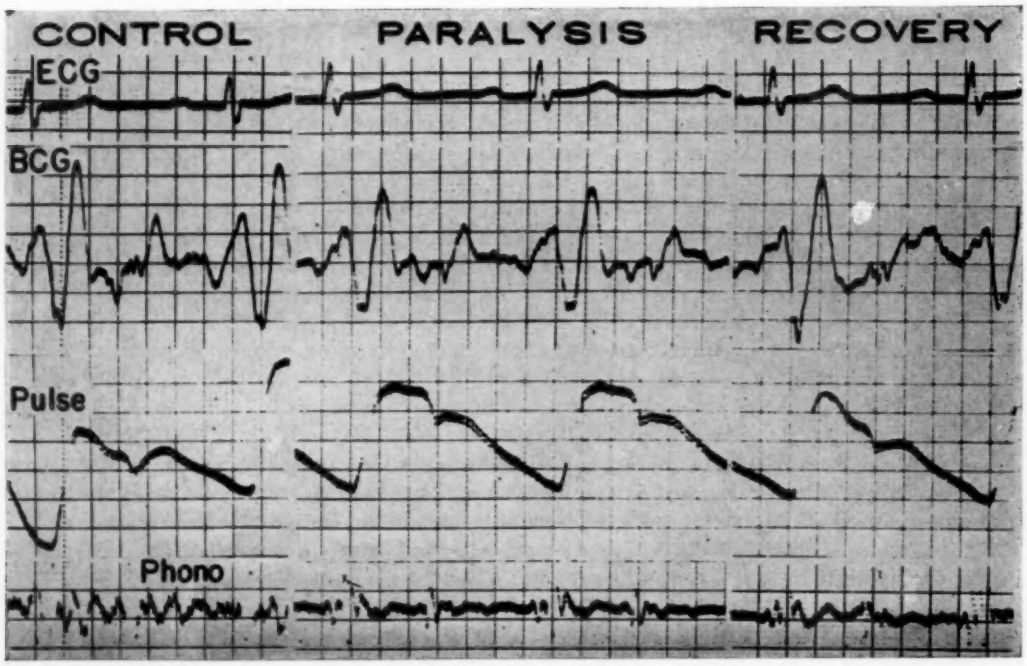

Fig. 2.—Electrocardiogram, ballistocardiogram, carotid pressure pulse, and phonocardiogram in Subject II during the control period, paralysis, and recovery. Paper speed, 50 mm./sec.

RESULTS

Subject I manifested no change in the amplitude of the I and J waves (100 and 98 per cent of control value, respectively) during paralysis (Fig. 1). The pulse rate, however, increased from 67 to 86 per minute, causing the systolic complexes of one beat to come hard upon the diastolic complexes of the beat preceding it, and allowing no time for return to the base line. (Thus, the resulting chaotic appearance of the record is probably not so meaningful as it first appears.) The record was still normal during muscular relaxation, but there seemed to be more high-frequency activity, and the I^+ wave was more prominent than in the control. The H and J peaks were slightly more rounded, and the amplitude was a little smaller in the recovery period than in the control, but the record at this time was also normal.

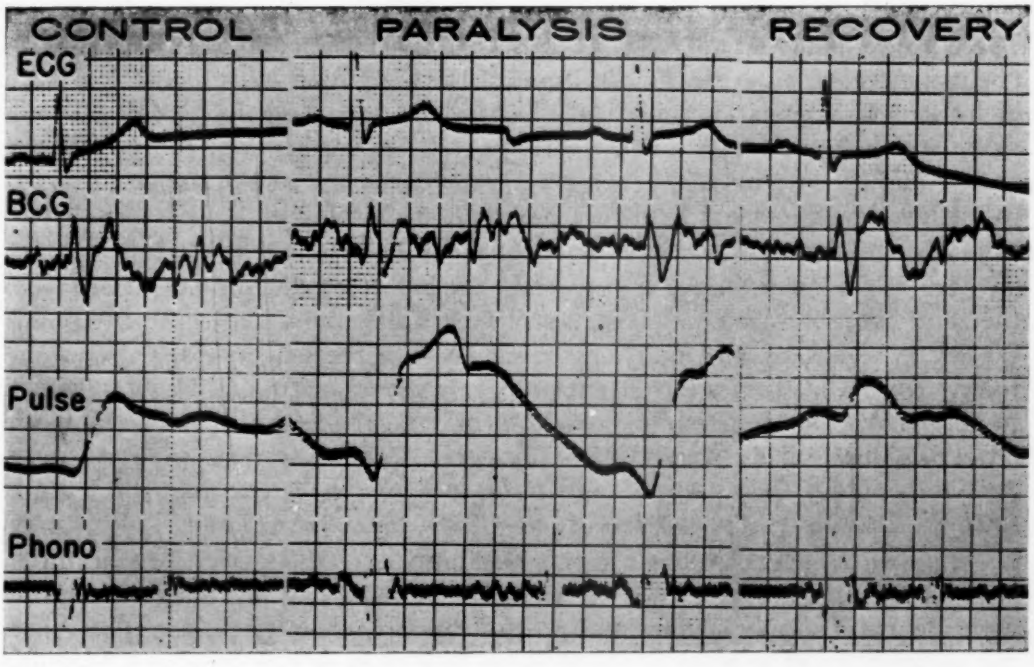

Fig. 3.—Electrocardiogram, ballistocardiogram, carotid pressure pulse, and phonocardiogram in Subject III during the control period, paralysis, and recovery. Paper speed, 50 mm./sec.

A few very high-frequency waves (40 per second) were lost from the ballistocardiogram of Subject II during paralysis, and the amplitudes of the I and J waves were somewhat diminished, to 66 and 74 per cent of the control, respectively. Otherwise the records were comparable to the control records (Fig. 2). No essential wave form was lost, and none was added. The recovery record was comparable to the control in every way.

The ballistocardiogram of Subject III became abnormal during paralysis (Fig. 3). The I wave was depressed to 67 per cent of the control value, and the J wave to 41 per cent; prominent late systolic forces resulted in a J_D wave. The

J wave was still depressed during recovery (59 per cent of control), but otherwise the pristine ballistic state was regained. A change in the carotid pulse contour occurred during paralysis and persisted through recovery.

DISCUSSION

The elimination of muscular tone did not materially affect the ultralow-frequency ballistocardiogram in 2 of the 3 subjects tested. The only changes noted were a slightly reduced prominence of a few very high-frequency waves and the I and J waves. Scarborough[12] points out that this result is not unexpected, because succinylcholine may not affect the behavior of the dorsal body "spring" even though it induces general muscular relaxation. Even if succinylcholine did affect the "spring," the effect should be small, for the ultralow-frequency suspension minimizes the importance of the "spring." The absence of some high-frequency waves during relaxation is not necessarily significant. These waves lie at the upper limit at which the ballistocardiogram records with fidelity; moreover, a decrease in stiffness of the body may have served to reduce high-frequency parasitic oscillations.[13] Muscular tone, therefore, did not seem to be a significant factor in preventing good linkage between the circulatory system and the internal and external body networks in 2 of the subjects coupled to an ultralow-frequency ballistocardiograph with shoulder straps. The effect of muscular relaxation on coupling without straps was not investigated.

The explanation for the disruption of the ballistocardiographic pattern from the third subject is obscure. One possibility is that blockade of the autonomic cardiac synapses by succinylcholine[14] somehow depressed myocardial contractility. Another is that intermittent positive pressure of 10 mm. Hg was enough to derange cardiac function.[15-17] Neither may be the real explanation, but the latter is a more likely possibility. Any agent specifically depressing the myocardium would probably affect the I wave to a greater extent than the J wave, since the I wave reflects ejection of blood from the myocardium.[10]

An additional consequence of this work applies to the study with anesthesia and the ballistocardiograph.[11] The degree of muscular relaxation associated with the use of succinylcholine was probably greater than that induced by ether; the impairment of venous return through lack of muscular tone and pumping action was certainly as great. The absence of the severe depression of the I wave seen with ether adds weight to the contention that the depressant effect of ether as shown by the ballistocardiograph is central and not peripheral.

SUMMARY

Ballistocardiograms were recorded on 3 subjects coupled to an ultralow-frequency ballistocardiograph by shoulder straps and totally paralyzed with succinylcholine. In 2 of the subjects, only minor changes from the control record were noted. The record in the third subject became abnormal, probably as a result of impaired cardiovascular function induced by positive pressure respiration. It is concluded tentatively that normal muscular tone does not interfere with the recording of the ultralow-frequency force ballistocardiogram.

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The Influence of Anticoagulant Therapy on the Occurrence of Cardiac Rupture and Hemopericardium Following Heart Infarction. I. A Study of 89 Cases of Hemopericardium (81 of Them Cardiac Ruptures)

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Spontaneous rupture of the heart was first described by William Harvey, in 1647 (cited by Edmondson and Hoxie[4]). As a curiosity it may be worth mention that Morgagni, who, in 1765, collected 10 cases of cardiac rupture and added one personal observation "made upon a most powerful monarch," himself died of the same cause.

In 1859, in Sweden, Malmsten[13] reported a case of cardiac rupture autopsied by Düben, in which the rupture for the first time was put in relation to a softening of the myocardium due to coronary thrombosis.

In Norway, rupture of the heart was first reported by Voss[18] at a meeting of the Society of Medicine in Christiania (Oslo) in 1867. A 74-year-old woman died after one day of illness characterized by oppression, dyspnea, and vomiting. Autopsy showed atheromatosis of the anterior coronary artery and softening of the anterior part of the wall of the left ventricle, with a 9 mm. long rupture in the involved area. On the same occasion Voss mentioned that the Pathologic Museum possessed two specimens of cardiac rupture received in 1848 and 1852, from Dr. Blich in Drammen. Additional cases of cardiac infarction with associated rupture were reported by Lund[11] and Tiedemand,[17] in 1869, and by Heiberg,[6] in 1870.

Krumbhaar and Crowell,[9] in 1925, collected 632 cases from the literature and added 22 others. They emphasized that the condition nearly always is related to coronary disease, and that it usually occurs in an acute infarct of the anterior wall of the left ventricle. Occasionally the rupture may have another pathogenesis, e.g., gumma or tuberculosis of the myocardium, bacterial endocarditis, echinococcus cysts, or malignant growths.

Large series were later published as follows: 40 cases by Benson, Hunter and Manlove[2] (1933); 72 cases by Edmondson and Hoxie[4] (1942), of which 13 had rupture of the interventricular septum; 26 cases by Munck[14] (1946) in a medicolegal series comprising 500 cases of sudden cardiac death; 80 cases by Oblath, Levinson and Griffith[15] (1952); 79 cases with hemopericardium, including 40

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with rupture, by Waldron, Fennell, Castleman and Bland[19] (1954); and 21 cases by Mather, Mallory and Laurenzi[12] (1956). The report by the last-mentioned authors includes a comprehensive list of references.

Atrial rupture is a much rarer occurrence than ventricular rupture and was first described by Rutherford, in 1828. Kohn, Harris and Gorham,[8] in 1954, collected from the literature 79 cases of atrial rupture, several of which were traumatic.

According to Gould[5] (1953), acute fatal myocardial infarctions are complicated by cardiac rupture in about 8 per cent of the cases. Physical effort has been stressed as a common contributory cause (Benson and associates[2]), and this seems to explain the much higher incidence of cardiac rupture among mental patients with acute infarction (Jetter and White[7]). Cardiac rupture occurs more often in women than in men (Edmondson and Hoxie[4]). Fatal myocardial infarction in young individuals is seldom complicated by cardiac rupture. Out of 450 autopsies of men who died of coronary disease between the ages of 18 and 39 years, Yater and associates[20] found only 4 cases of cardiac rupture (0.9 per cent). Atrial rupture is relatively more common in younger patients than the usual type of heart rupture (Clowe, Keilert and Gorham[3]).

PERSONAL INVESTIGATIONS

In a subsequent article we will give an account of the frequency of cardiac rupture in patients receiving anticoagulant therapy for heart infarction, as compared to that in untreated patients. The primary series in the present study is almost identical with that in the subsequent article, comprising 1,303 patients who died of heart infarction. The present study is concerned with 89 cases of hemopericardium found at autopsy.

MATERIAL

During the period from Jan. 1, 1945 to July 1, 1956, a total of 1,303 patients died of myocardial infarction in Medical Departments VII, VIII, and IX of Ullevål Hospital. Autopsy was performed in 1,229 cases (94.3 per cent) which constitute the primary material. Hemopericardium was found in 41 men and 48 women, totaling 89 cases, or 7.3 per cent of the autopsies. Of these, 5 had hemopericardium without rupture and 3 had rupture of the ascending aorta, while the remaining 81 cases, or 6.6 per cent of the autopsied cases, had myocardial rupture. The 41 men were aged 41 to 86 years, with a mean of 68.5 years; the women were aged 55 to 90 years, with a mean of 72.5 years, i.e., 4 years more than in the male group. Myocardial rupture was not found n men under 50 years of age and in women under 60 years. Age distribution is shown in Table I.

From Table I it will be seen that most cases of hemopericardium with myocardial or aortic rupture (53 out of 84) occurred in the age group 60 to 79. Under 60 years of age there was a considerable majority of males, while over 80 years of age the females prevailed. This accords with the age distribution of patients with myocardial infarction as collected from Ullevål Hospital.[1]

Previous Coronary Disease and Other Complicating Conditions.—Twenty-nine patients had a history of previous angina pectoris, and 3 had had infarction earlier. Forty-six patients had not had symptoms of angina pectoris; in 8 cases adequate information was not available. Hypertension was a common occurrence, and many patients had suffered from hypertensive heart disease for several years prior to infarction. Thirty-three patients had blood pressure readings over 160 mm. Hg systolic after admission, and 30 had readings over 100 mm. Hg diastolic. Aortic

valvular stenosis was present in 6 patients, and one of them had mitral stenosis as well. Syphilitic aortitis was present in 1 patient and inveterate syphilis in 1 patient. Serologic tests for syphilis had been carried out in 57 of the patients and were negative in all instances, including the 2 cases mentioned above. Seven patients (7.6 per cent) had diabetes mellitus.

TABLE I. AGE DISTRIBUTION OF 89 PATIENTS WITH HEMOPERICARDIUM*

AGE	40–49	50–59	60–69	70–79	80–89	90 AND OVER	TOTAL
Men	(1)	11	10 + (1)	13	5		39 + (2)
Women		2 + (1)	14 + (1)	16 + (1)	11	2	45 + (3)
Total	(1)	13 + (1)	24 + (2)	29 + (1)	16	2	84 + (5)

*Figures in parentheses denote hemopericardium without rupture of the heart or aorta.

A study of height-weight ratios did not reveal any particular relation between overweight and cardiac rupture.

Treatment with anticoagulants was given to 33 patients (37 per cent), while the remaining 58 either received no anticoagulant or died so early that they must be considered untreated, since heparin was given only occasionally during the first day of illness. Table II shows the number of treated and untreated men and women in different age groups. Of patients above 80 years of age, only 3 received anticoagulant therapy. Furthermore, it will be seen that hemopericardium without rupture occurred only in the treated group.

TABLE II. ANTICOAGULANT THERAPY IN RELATION TO AGE GROUPS IN 89 PATIENTS WITH HEMOPERICARDIUM*

AGE		40–49	50–59	60–69	70–79	80–89	90 AND OVER	TOTAL
Men	Treated	(1)	3	5 + (1)	6	1		15 + (2)
	Untreated		8	5	7	4		24
Women	Treated		(1)	5 + (1)	6 + (1)	2		13 + (3)
	Untreated		2	9	10	9	2	32
Total	Treated	(1)	3 + (1)	10 + (2)	12 + (1)	3		28 + (5)
	Untreated		10	14	17	13	2	56

*Figures in parentheses denote hemopericardium without rupture of the heart or aorta.

The clinical duration of the infarct, i.e., the interval between infarction and rupture (death) varied greatly, as shown in Fig. 1, which also shows the distribution of treated and untreated cases. Over 30 per cent of the patients died during the first day of illness (some were already dead, others moribund at the time of admission). In some of these cases with a short history of illness or sudden death without previous illness, autopsy showed an infarct of some time's standing. The figures are therefore hardly quite reliable as to the exact duration of the infarct at the time of death. More than half of the cases (51) died during the first five days, and about 80 per cent (73) died during the first ten days. Of those receiving anticoagulant therapy two thirds (22 of 33) died during a period from the fourth to ninth day.

Site of Rupture.—In all of our 81 cases the rupture was of the left ventricle; in most instances the rupture was near the apex, while in others it was close to the interventricular septum, which, in that event, usually was involved as well. Perforation of the interventricular septum was demonstrated in 1 case. In 43 cases the rupture involved the anterior wall, in 29 cases the posterior wall, in 1 case the lateral wall, and in 8 cases the apex. As mentioned previously in the text, 3 patients had rupture of the ascending aorta; in one it was situated just above the aortic valve, in another 4 cm. above, and in a third 5 cm. above. In the last-mentioned case the infarction was obviously secondary to the rupture; there was an egg-sized aneurysm extending from the rupture to the valve, with resultant occlusion and thrombosis of the right coronary artery.

The size of the rupture varied from an opening barely permitting a thin probe to coin-sized openings or to tears up to 4 cm. in length.

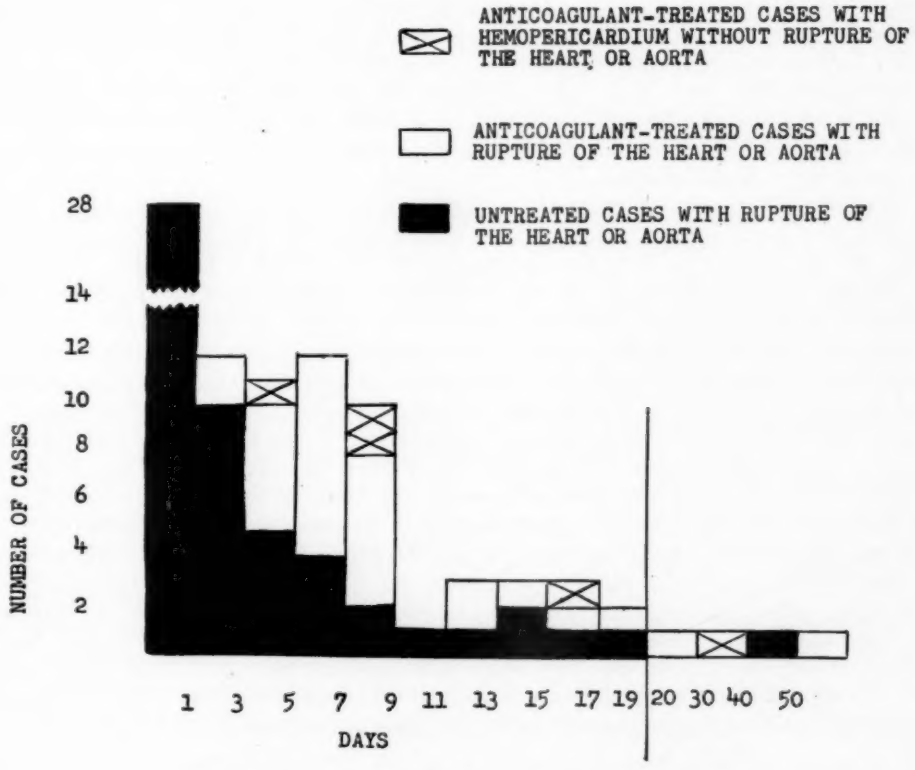

Fig. 1.—Interval between infarction and rupture (death).

The gross appearance of the myocardium in the affected area largely depended on the duration of the infarct. It was described partly as being mottled yellowish grey, often infiltrated with extravasated blood, and partly as necrotic and mollified, occasionally also fibrotic. Fibrosis occasionally involved large areas, probably representing old infarctions; in other instances it showed a patchy distribution, giving the myocardium a speckled appearance. In some cases the heart muscle in the involved areas was reduced to a thin membrane. Three patients had aneurysm of the heart. In one of these cases, in which the aneurysmal dilatation of the left ventricle had been demonstrated roentgenologically, there was an interval of 54 days between infarction and rupture.

Considerable hypertrophy of the heart, probably resulting from long-standing hypertension, was found in several instances. In 39 men the weight of the heart varied from 380 to 900 grams, averaging 540 grams; 19 of them had heart weights over 500 grams. In 46 women the weight of the heart varied from 260 to 690 grams; 24 of them had heart weights over 400 grams.

Coronary lesions were demonstrated in all instances. The lesions were reported partly as atheromatosis, partly as sclerosis, and were usually associated with partial or complete occlusion of the affected vessel. More than half of the cases had occluding coronary thrombosis. In 2 cases the relevant branch was described as normal.

The amount of blood in the pericardial cavity varied from 100 to 1,000 ml., averaging about 350 ml. In the case of an 82-year-old woman who was dead on admission the pericardium contained only 100 ml. of blood. There was a tear 2 cm. long in the posterior wall, covered by a thin layer of fibrin, with formation of a nut-sized clot corresponding to the site of the rupture. This was obviously a case of "protected" rupture. Similar findings were made in a 66-year-old man. In this patient, as well, the pericardium contained only 100 ml. of blood, and the rupture was found "after removal of the coagulum." Thus there was a certain degree of "protection," so that a definite heart tamponade had obviously not existed.

No definite difference between the two groups was found with regard to the nature of the pericardial contents and the distribution of liquid contra coagulated blood. Nor was there any difference between the groups regarding the pericardial blood volume.

Anticoagulant Therapy.—Anticoagulant therapy was given to 33 patients and was initiated in a few more, but these patients died so early that the treatment may be considered ineffective. Dicumarol was used in 24 cases; 9 of these received heparin initially. The remaining 9 patients were treated with phenylindandione.

The anticoagulant treatment was checked by estimation of the prothrombin-proconvertin level (PP value) by the method of Owren, and in some instances by estimation of the prothrombin index by the method of Quick. In the treated group all except 2 had such estimations carried out during the last two days of life, viz., on the day of death in 6 cases, one day prior to death in 17 cases, and two days prior to death in 8 cases.

Table III shows the values last registered in the treated group. It will be seen that 16 of the 33 patients were in a therapeutic range of anticoagulant effect (PP values between 10 and 30 per cent of normal), while 8 had values above 30 per cent and 8 under 10 per cent. In these last cases the values were 7, 6, 6, 5, 4, 4, and 3 per cent, respectively. In the 10 to 20 per cent group there were many values between 10 and 12 per cent. In 2 cases the second last PP values registered were under 10 per cent. It is also likely that the value at the time of death in some instances might have been lower than the last registered one. In the patients with hemopericardium without rupture the PP value in 3 cases was 11,47 and 90 per cent, respectively, and in 2 cases the prothrombin index was 17 and 24 per cent, respectively. The one whose prothrombin index on the day prior to death was 17 per cent had had massive hematuria for two days. In another patient, a woman treated with Dicumarol during the entire period of hospitalization, PP values as registered on three occasions about three weeks prior to death were 11, 12, and 12 per cent, respectively. Occult blood occurred in the feces, and injections of vitamin K were given on the eighteenth day prior to death, whereupon the PP value was constantly above 30 per cent.

TABLE III. LAST REGISTERED PP VALUES IN 33 CASES OF HEMOPERICARDIUM RECEIVING ANTICOAGULANT THERAPY

PP VALUE (%)	<10	10–19	20–29	30–39	40–49	50 AND OVER	UNKNOWN
Number of Cases	8	12	4	3	2	3	1

All the patients except one in the present series died suddenly. The one exception was a 79-year-old woman who died after seven days of illness. Thirty-five minutes before death she fell unconscious with Cheyne-Stokes respiration. In the autopsy report the rupture was described as "small," and the pericardial cavity contained only 200 ml. of partly coagulated blood. The possibility thus exists that there had been only a gradual leakage and not a sudden, larger hemorrhage.

A precipitating cause of the rupture was not demonstrable in the majority of cases. One woman died suddenly on the seventh day of illness when she left the bed to go to the toilet; another patient collapsed following administration of an enema, and one patient died immediately after infusion of normal saline.

DISCUSSION AND CONCLUSION

The present series has been studied with a view to elucidating the problem concerning the occurrence of cardiac rupture or hemopericardium in patients with myocardial infarction under anticoagulant therapy. Insofar as we can determine, this is the largest series of cardiac ruptures published to the present time, and, therefore, we have focused our attention on this complication in general. Our observations accord closely with those published by other authors. The incidence of hemopericardium (7.3 per cent) and cardiac rupture (6.6 per cent) is in accord with other recent studies. There is a female preponderance (44 women to 37 men) in the present series despite the prevalence of myocardial infarction in males in the total infarct material.

The age and sex distribution is in close agreement with that found by Oblath and associates[15] in a similar American series.

The present study indicates that hemopericardium with or without cardiac rupture might be related to anticoagulant therapy. The low PP values antecedent to rupture merit special attention. Among the 89 cases of hemopericardium there were 8 with excessive anticoagulant effect (under 10 per cent prothrombin-proconvertin activity). The high sensitivity to anticoagulants often seen in the presence of cardiac insufficiency and in severely exhausted patients might be the cause of excessive anticoagulant effect.

Secondly, it is noteworthy that all of the 5 patients with hemopericardium without rupture were found in the treated group. Excessive anticoagulant effect did not exist shortly before death in any of these cases. Of course there is a possibility that excessive anticoagulant effect might have existed earlier during treatment in these cases. Considering the marked infiltration of extravasated blood into the area of a recent myocardial infarction or rupture, it is easily realized that a decreased coagulability of the blood is a factor of great importance. Furthermore, it is a well-known experience that hemorrhage is a not infrequent occurrence in patients above the upper therapeutic limit of anticoagulant effect (prothrombin-proconvertin activity above 30 per cent). Experience gained from long-term treatment of angina pectoris or nonfatal myocardial infarction seems to indicate that 50 to 30 per cent prothrombin-proconvertin activity may afford nearly as good "protection" as a 30 to 10 per cent level. If we, in the 33 treated patients with hemopericardium, discredit the anticoagulant treatment in the 5 patients who died with hemopericardium without rupture, plus the 8 patients who had very low PP values just prior to death, plus 2 patients whose second last PP values before death were under the lower therapeutic limit, it cannot be excluded that the anticoagulant therapy might have been a contributing cause of death in 15 cases.

It has been emphasized by Scherf[16] that in patients with cardiac infarction and associated rupture the escape of blood into the pericardial cavity may be very slow, so that an impending heart tamponade may be diagnosed clinically.

In that event, aspiration of the accumulated blood may be lifesaving. Symptoms indicative of such a development were not observed in any of the cases in the present series. All patients except one died suddenly. We are inclined, therefore, to believe that leaking hemorrhages in impendlng rupture are exceedingly rare.

Our conclusion is that a fatal hemopericardium may occasionally be caused by anticoagulant therapy in myocardial infarction, even in patients within a "safe" range of anticoagulant effect. A number of cases with excessive anticoagulant effect sustained cardiac rupture. In these cases an overdosage of anticoagulant or excessive anticoagulant effect seems to have precipitated a fatal cardiac rupture.

SUMMARY

Among 1,303 cases of fatal cardiac infarction, with an autopsy rate of 94 per cent, 89 cases of hemopericardium were found at autopsy. Of these, 81 had myocardial rupture, and 3 had rupture of the aorta; in the remaining 5 cases localized cause could not be demonstrated. These 5 cases occurred among the 33 patients receiving anticoagulant therapy. In this group there were 8 with excessive anticoagulant effect shortly before death. In addition, there were at least 2 patients who had excessive anticoagulant effect at an earlier stage of treatment. Observations in the present series indicate that anticoagulant therapy increases the risk of hemopericardium with or without cardiac rupture, largely because of an overdosage of anticoagulants.

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The Influence of Anticoagulant Therapy on the Occurrence of Cardiac Rupture and Hemopericardium Following Heart Infarction. II. A Controlled Study of a Selected Treated Group Based on 1,044 Autopsies

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Anticoagulant therapy in myocardial infarction has now been used for so many years that nearly complete agreement seems to exist about the indications, at least as far as short-term therapy is concerned. The Quick and Owren methods for estimation of the prothrombin time and prothrombin-proconvertin level, respectively, have contributed greatly to minimize the danger of bleeding, and this complication is now comparatively rare. Still it happens occasionally that patients with acute myocardial infarction die of heart tamponade due to hemopericardium. The commonest cause of hemopericardium is rupture of the myocardium, but in some instances it may be a "hemorrhagic pericarditis" without rupture. Thus, the question arises as to whether a hemopericardium or heart rupture might be related to anticoagulant treatment.

During recent years observations have been made which indicate that anticoagulant therapy in patients with acute myocardial infarction increases the risk of death from rupture or hemopericardium. A clarification of this problem is of great importance. It was thus considered that a study of autopsied cases of myocardial infarction, including patients receiving anticoagulant therapy as well as patients receiving no anticoagulant therapy, might throw some light upon the problem.

This article is a clinical supplement to the preceding study of 89 cases of hemopericardium.[1]

REVIEW OF THE LITERATURE

Wright and associates,[9] in 1954, reported that among 589 treated cases 16 per cent died within six weeks, as compared to 23.4 per cent of 442 cases in a control group receiving no anticoagulant; 4.1 per cent of all treated cases and 2.4 per cent of all untreated cases died with heart rupture or hemorrhage (mostly hemopericardium) as an immediate or contributing cause of death. It was estimated, therefore, that if this difference is typical, and not due to chance, the risk that anticoagulants under otherwise comparable conditions will contribute to the death of the patient is about 1.7 cases per 100 treated with anticoagulants.

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Howell and Kyser[5] found 8 cases of myocardial rupture among 132 autopsied patients who died of cardiac infarction after more than three days of illness; 5 of these ruptures occurred among 98 untreated patients and 3 among 34 patients treated with anticoagulants.

Waldron and associates,[8] in 1954, found 79 cases of hemopericardium among 545 autopsied patients who died of acute cardiac infarction in Massachusetts General Hospital, during the period from 1932 to 1951. There was a threefold increase of the incidence of hemopericardium and at least a twofold increase of the incidence of myocardial rupture (40 cases) in the anticoagulant-treated group as compared with the untreated group.

McQuay and associates,[6] in 1955, found 20 cases of myocardial rupture among 133 autopsied patients who died of acute cardiac infarction. Of these, 93 had transmural infarcts, and all the ruptures were found in this group. Among 23 patients treated with anticoagulants there were 6 ruptures, as compared to 14 ruptures among 70 untreated patients.

Mather and associates,[7] in 1956, found 21 ruptures among 183 autopsied cases of acute myocardial infarction. Of 13 patients under effective anticoagulant therapy 3 sustained rupture; of 32 cases in which anticoagulant treatment was attempted there were 6 ruptures, while 15 of the 146 patients who received no anticoagulant had cardiac rupture. The difference between the two groups is not statistically significant.

PERSONAL INVESTIGATIONS

The primary material includes all autopsied patients who died of myocardial infarction in Medical Departments VII, VIII, and IX of Ullevål Hospital, during the period from Jan. 1, 1945 to July 1955.*

We knew that most of the untreated cases (control group) would be found in the period from 1945 to 1950, i.e., before anticoagulant therapy was generally adopted. After that time the method of Owren for estimation of prothrombin-proconvertin activity (PP value) was substituted for the method of Quick for estimation of the prothrombin time.

The treatment of cardiac infarction had otherwise followed the same principles in the three departments and had not been altered during the period mentioned, save with the exception that patients admitted during the last part of the period were allowed to leave the bed somewhat earlier, and that shocked patients in some instances were treated with noradrenalin (none of those, however, were included in the series of selected cases).

Possible dissimilarities between the treated group and the untreated control group were eliminated, to a major extent, because the selection of the latter group was extended to the period from 1945 to 1953, inclusive (Department VII).

The criteria for "effective" (adequate) anticoagulant therapy had to be very strict, and in order to get a material as "pure" as possible, we decided to exclude the following categories of cases in both groups: (1) patients in whom the infarct had not been diagnosed during life, and who consequently had received no anticoagulant; (2) patients showing old infarction; (3) patients in whom the exact time of occurrence of the infarction was not definitely known; and (4) patients who died before reaching a therapeutic range of anticoagulant effect, i.e., within four days after admission.

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*We wish to express our thanks to the Heads of the three departments, Professor R. Hatlehol, Professor C. Müller, and Professor H. J. Ustvedt, and to the Head of the Department of Pathology, Prosector E. Hval, for their permission to use the records of the respective departments.

During the period mentioned, a total of 1,110 patients died of cardiac infarction in the three departments. Autopsy was not permitted in 66 cases. The autopsy rate was thus 94 per cent, and the primary series included a total of 1,044 autopsied cases.

After having examined the records of Medical Department VII up to 1954, we had collected 72 cases which fulfilled the criteria mentioned above. These patients, 38 men and 34 women, had not been treated with anticoagulants and were considered as suitable controls. Since we knew that the treated group would not be so large, we stopped further collection of controls. From the records of the three medical departments for the period from Jan. 1, 1945 to Dec. 31, 1954, we collected 53 treated cases, 40 men and 13 women. The treated and untreated male groups thus included a similar number of cases (40 and 38, respectively), but the treated group of women was critically small (13 cases). Therefore, an analysis of the material was postponed so that the collection of treated female cases could be continued.*

By the end of June, 1956, the treated group of women had been increased by 16 cases. The treated group then comprised 40 men and 29 women, i.e., a total of 69 cases, and the control group comprised 38 men and 34 women, i.e., a total of 72 cases.

Age distribution is shown in Table I.

The average age for the men in the treated group was 65.3, in the control group 66.1 years, i.e., 0.8 year higher in the control group. The corresponding means for the female groups were 74.8 and 75.5 years, i.e., 0.7 year higher in the control group. None of the women was below 60 years of age, and the male-female age difference was 9.5 years in the treated group and 9.4 years in the control group.

The duration of the disease is shown in Table II.

TABLE I. AGE DISTRIBUTION OF 69 ANTICOAGULANT-TREATED PATIENTS AND 72 UNTREATED PATIENTS WITH FATAL MYOCARDIAL INFARCTION

AGE (YEARS)		<50	50–59	60–69	70–79	80 AND OVER	TOTAL
Men	Treated	1	7	12	18	2	40
	Untreated	2	6	10	15	5	38
Women	Treated			3	16	10	29
	Untreated			6	16	12	34
Total	Treated	1	7	15	34	12	69
	Untreated	2	6	16	31	17	72

*This was done after consulting the Life Insurances' Institute for Medical Statistics of the Oslo City Hospitals. This institute has studied the same infarct material from different angles (Acta med. scandinav., Suppl. 315, 1956) and considered it unlikely that the incorporation of an additional number of treated female cases would represent any source of error.

From Table II it will be seen that the majority of deaths occurred during the first three weeks after onset of infarction. Seventy per cent of the deaths in the treated group and 64 per cent in the control group occurred within twenty days after infarction. From the table and from Fig. 1 it will be seen, also, that almost 50 per cent of the patients in the control group died within five to nine days, while there was a greater variation in the length of survival in the treated group. This, we believe, might be related to the routine discontinuance of anticoagulant therapy after four weeks. Immediate rise in temperature and subsequent death ensued in a number of patients when anticoagulant therapy was stopped.

TABLE II. INTERVAL BETWEEN INFARCTION AND DEATH IN 69 ANTICOAGULANT-TREATED PATIENTS AND 72 UNTREATED PATIENTS WITH MYOCARDIAL INFARCTION, INCLUDING 23 CASES OF HEMOPERICARDIUM WITH OR WITHOUT RUPTURE*

DAYS		5-9	10-14	15-19	20-24	25-29	30-39	40-49	50-59	60 AND OVER	TOTAL
Men	Treated	7(5)	11(1)	14(3)	2	0	6	0	0	0	40(9)
	Untreated	17(1)	3	3	3	4	3	1	1	3	38(1)
Women	Treated	5(4)	6(1)	5(1)	3	3	2	2	1	2	29(6)
	Untreated	16(5)	2	6(1)	3	1	2	2(1)	0	2	34(7)
Total	Treated	12(9)	17(2)	19(4)	5	3	8	2	1	2	69(15)
	Untreated	33(6)	5	9(1)	6	5	5	3(1)	1	5	72(8)

*Figures in parentheses denote cases of hemopericardium with or without rupture.

The incidence of hemopericardium and myocardial rupture will also be seen from Table II. In the present series there was only a single case of hemopericardium without rupture. These two conditions, therefore, are considered collectively in the text. The case mentioned was that of 41-year-old man who died after seventeen days of anticoagulant treatment with Dicumarol. The PP value on the day prior to death was 11 per cent.

From the tables it will be seen that 15 of the treated patients, or 21.7 per cent, and 8 of the untreated patients, or 11 per cent, died of cardiac rupture. Seven of these 8 patients were women. Definite differences between the two groups were also noted with regard to the occurrence of other lesions of the pericardium.

Hemorrhagic fluid with or without fibrin deposits was found in 10 patients in the treated group (14.5 per cent) as compared to 4 patients in the control group (5.5 per cent). Serous fluid, on the other hand, was found in 8 patients (11.6 per cent) of the treated group and in 18 patients (25 per cent) of the control group. Normal pericardium was found in 22 patients (32 per cent) of the treated group and in 31 patients (43 per cent) of the control group.

Intracardiac mural thrombi were found less frequently in the treated group (4 cases or 6 per cent) than in the control group (8 cases or 11 per cent). Dicumarol was used as anticoagulant in 49 cases and phenylindandione in 20. For

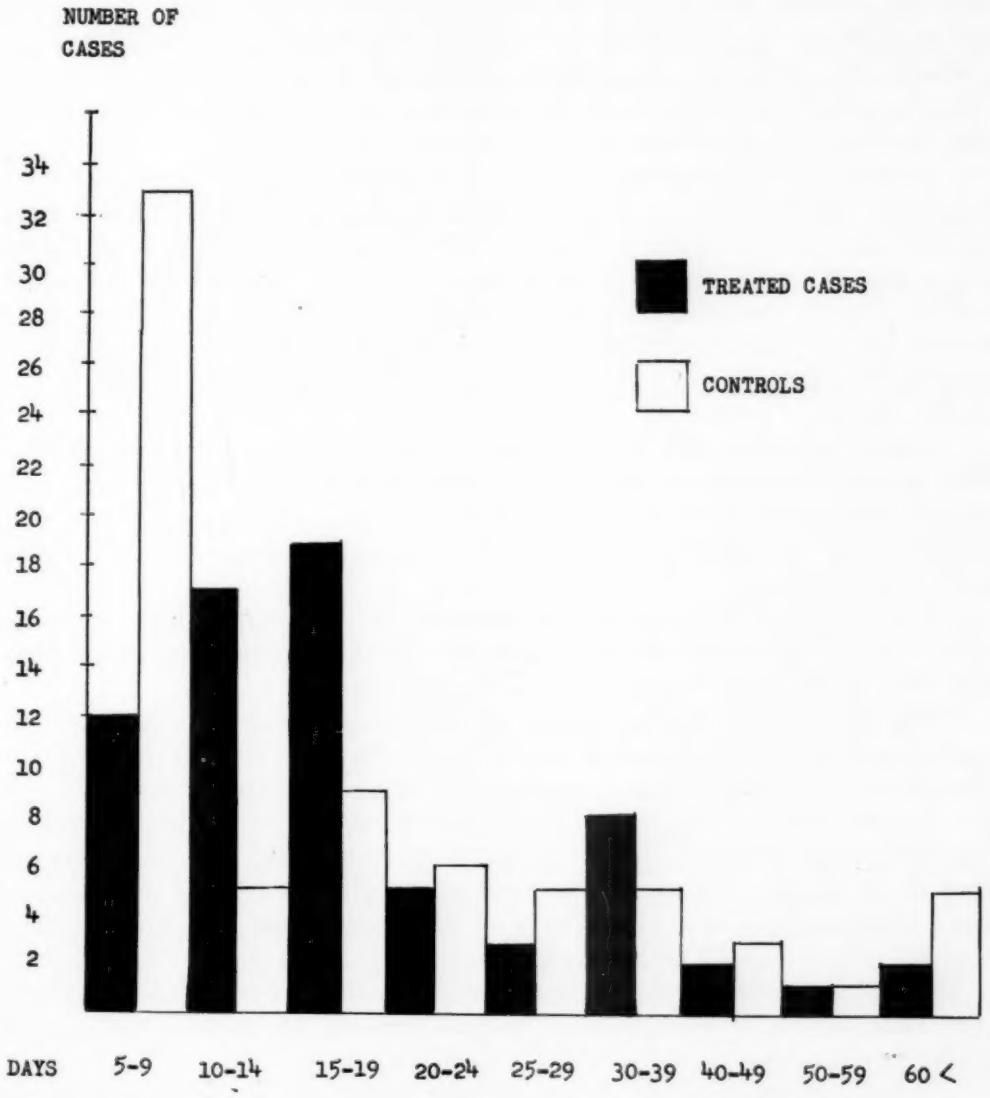

Fig. 1.—Interval between infarction and death;

estimation of prothrombin activity, use was made of Quick's method in 10 cases and of Owren's method in the remaining 59. Prothrombin levels prior to death and the occurrence of hemopericardium in relation to these have been commented upon in the preceding article.

DISCUSSION AND CONCLUSION

The present series is considered suitable for an analysis aimed at an elucidation of the problem concerning hemopericardium in relation to anticoagulant therapy. First of all, the primary material is sufficiently large and representative, with an autopsy rate of 94 per cent, a figure hardly exceeded in other materials. Secondly, the selection of cases according to the criteria mentioned has brought out two groups, viz., one treated group and one control group, which are comparable with regard to sex and age distributions.

Concerning the incidence of hemopericardium or rupture, a marked difference between the two groups was demonstrated.

Fifteen of the 69 patients in the treated group had hemopericardium, as compared with 8 of the 72 patients in the control group. The incidence of hemopericardium was consequently twice as large in the treated group as in the control group. The difference was most spectacular when the male cases were considered alone. Including both sexes, however, the difference between the two groups was not statistically significant. Still it seems to be real in view of the definite difference in the occurrence of hemorrhagic pericardial effusion contra serous effusion.

The assumption that the difference between the two groups might be related to the anticoagulant therapy, and that adequate anticoagulant effect was largely accomplished, is also indicated by the lower incidence of endomural thrombi in the treated group, viz., 4 of 69 cases, as compared to 8 of the 72 cases in the control group.

Data reported in the literature indicate that the risk of heart rupture is about 1.5 to 2 times as great among patients in a therapeutic range of anticoagulant effect as among patients receiving no anticoagulant.

The incidence of cardiac rupture in the present series accords closely with figures reported by other authors, even though the cases included in the present series were selected according to other and perhaps more strict criteria.

In the report by Wright and associates,[9] as well as in that by Waldron and associates,[8] the incidence of hemopericardium without rupture was larger than that in our series. Cases of hemopericardium without rupture were found in the Ullevål material as well, but none of them, except one, was included in the selected series reported on in this article.

Our observations seem to permit the conclusion that anticoagulant therapy may contribute to a weakening of the affected area of the myocardium, with consequent rupture.

It has been suggested by Holten,[4] among others, that the anticoagulant therapy itself may bring in a moment of uncertainty when comparing series of treated and untreated patients. Some patients who without such therapy would have died early will now, because of the treatment, be brought through the first weeks, only to die later on of cardiac rupture. Against this point of view it may be held that the controlled study of Bjerkelund[3] has shown a significant difference in mortality only in men below the age of 60 years. This age group represents only 10 per cent of our series. In our opinion, therefore, the circumstances mentioned above will not influence our numbers to any notable degree.

SUMMARY

In 1,110 fatal cases of cardiac infarction, 1,044 autopsies were performed (autopsy rate, 94 per cent). All patients with inadequate anticoagulant effect, as well as those in other categories, were excluded. This left 69 patients receiving effective anticoagulant therapy. These were compared with a group of 72 control patients of corresponding age and sex. The incidence of hemopericardium (1 case) or myocardial rupture (14 cases) in the treated group was about twice as large (15 cases out of 69) as in the control group (8 cases out of 72).

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A Clinical Evaluation of Cross-Polar Plication (Posteromedial Annuloplasty) in the Surgical Treatment of Rheumatic Mitral Regurgitation

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INTRODUCTION

Failure of the mitral valve leaflets to coapt properly is a common aftermath of rheumatic activity. The defect, which may occur alone or in association with mitral stenosis or aortic valve disease, develops when the annulus dilates, when scarring and retraction lead to a deficiency of leaflet tissue, or when there is an unequal, fibrotic contracture of the supporting chordae.

The most significant incompetence of the mitral valve generally appears in the region of the posterior commissure where there is little reserve tissue to compensate for the overstretched annulus or the loss of leaflet substance (Fig. 1). Occasionally, when the cusps are markedly calcified, when the chordae are grossly contracted, or when subacute bacterial endocarditis has caused considerable endocardial destruction, the incompetence is not commissural but is central or extends across the entire line of valve closure.

Various surgical measures have been proposed to correct the lesion. The earliest effort merely sought to block the opening which persisted when the edges of the mitral leaflets failed to make secure contact.[1] This required the insertion of a pericardial tubular pedicled graft across the ventricular aspect of the valve. This procedure, and those patterned after it, were abandoned when it was established that the graft became fibrotic, shrunken, and incapable of blocking the ventricular-atrial regurgitation of blood.

Subsequently, a method was devised to enforce a more exact coaptation of the mitral cusps by passing a direct suture through the leaflets in the region of

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their greatest incompetence.[2] This method fell into disuse because the tension required to approximate the leaflets often led to serious lacerations or produced an unintentional but significant stenosis. Furthermore, the rigid, calcified valve always remained beyond the scope of this operation.

Fig. 1.—Photograph of autopsy specimen showing typical posteriorly located "tear drop" incompetence.

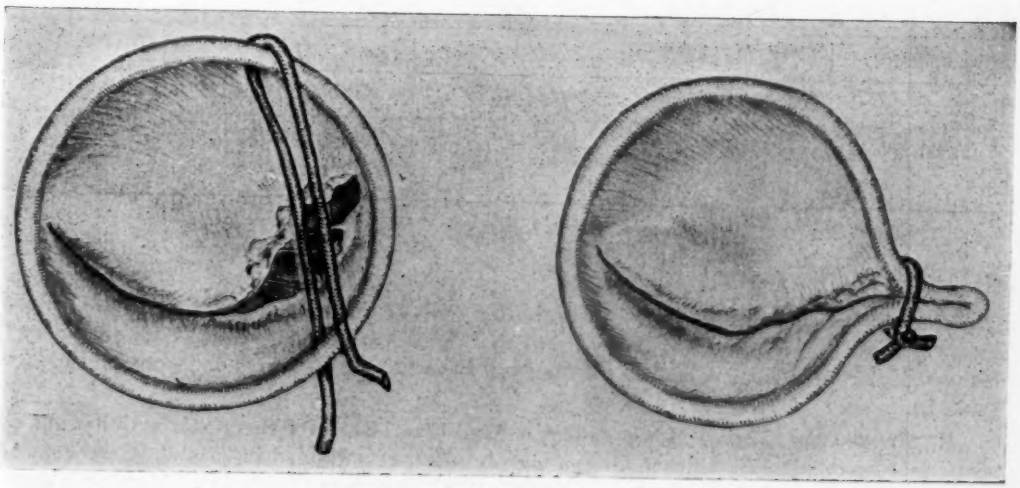


Fig. 2.—Technique of cross-polar plication. The suture displaces one leaflet closer to the other in the region of incompetence. Normal leaflet action is not compromised and mitral stenosis is not produced.

Current surgical practices are based on the concept that the incompetence can be corrected materially by reducing the circumference of the annulus. One of the suggested techniques requires encompassing and constricting the entire annulus.[3] A more recent measure termed cross-polar plication reduces the circumference by judiciously introducing a suture in the region of the posterior commissure[4] (Fig. 2).

The present report represents a critical evaluation of cross-polar plication as it has been applied to 40 patients who were operated on between Aug. 16, 1956 and June 24, 1957.

TABLE I. THE MATERIAL

	AGE					SEX		HISTORY OF RHEUMATIC FEVER		TOTAL CASES
	UNDER 20 YR.	20-30	30-40	40-50	OVER 50	MALE	FEMALE	YES	NO	
Number of cases	2	11	16	9	2	9	31	30	10	40

TABLE II. SYMPTOMATOLOGY

	SYMPTOMS			
	DYSPNEA	FATIGUE	PND	ANKLE EDEMA
Absent	4 (10%)	3 (7.5%)	20 (50%)	18 (45%)
Mild	13 (32.5%)	14 (35%)	10 (25%)	10 (25%)
Moderate	19 (47.5%)	19 (47.5%)	8 (20%)	10 (25%)
Severe	4 (10%)	4 (10%)	2 (5%)	2 (5%)
Total	40 (100%)	40 (100%)	40 (100%)	40 (100%)

MATERIAL

The 40 patients had pure mitral regurgitation with no evidence of mitral stenosis. In each instance the anatomic lesion was the result of past rheumatic activity and was not secondary to left ventricular dilatation. The ages ranged from 19 to 52 years. Thirty-one were female. (See Table I.)

1. *Preoperative Clinical Manifestations.*—A positive history of rheumatic activity was obtained in 30 patients. Significant fatigue and dyspnea, encountered in 37 and 36 patients, respectively, represented the most frequent subjective complaints (Table II). Manifestations of right heart failure, such as peripheral edema, were much less common. None of the patients had had previous embolic accidents. On auscultation (Table III) an apical systolic murmur was heard without exception. In the vast majority of the patients the intensity of the murmur was

at least Grade 3. The first mitral sound was of normal duration, pitch, and intensity in 30 patients (75 per cent). In the remainder the pitch was lower and/or the intensity diminished. A sharp first sound was recorded in 10 patients.

Radiographically, the over-all cardiac size was considered extremely enlarged in 20 patients (Table IV). Massive enlargement of the left atrium was observed in approximately the same number. It was most difficult to offer a precise estimate of right and left ventricular size. The most frequent electrocardiographic abnormality was auricular fibrillation, which was observed in 30 of the patients. Applying the criteria of the American Heart Association, 53 per cent of the patients were in either Class III or Class IV (Table V).

TABLE III. AUSCULTATORY FINDINGS

	NUMBER OF CASES	PER CENT
Apical Systolic Murmur		
Grade 1	—	—
Grade 2	2	5
Grade 3	32	80
Grade 4	6	15
Apical Diastolic Murmur		
Present	17	42.5
Absent	23	57.5
Mitral First Sound		
Normal or diminished	30	75
Sharp	10	25
Opening Snap		
Not present	33	82.5
Present	7	17.5
Accentuated P_2	30	75
Atrial Fibrillation	30	75
NSR	10	25

TABLE IV. RADIOLOGIC STUDIES

DEGREE	HEART SIZE	LEFT ATRIUM	PULMONARY ARTERY
Normal	0	0	4 (10%)
Grade I	2 (5%)	7 (17.5%)	9 (22.5%)
Grade II	18 (45%)	14 (35%)	17 (42.5%)
Grade III	16 (40%)	12 (30%)	10 (25%)
Grade IV	4 (10%)	7 (17.5%)	0

2. *Special Studies.*—Left heart catheterization was performed in 15 of the 40 patients. The contour of the left atrial pressure curve was consistent with the diagnosis of mitral regurgitation in 10 of these patients. A gradient across the mitral valve during the period of ventricular filling was not demonstrated in 12 of the patients, while the remainder of the group showed small gradients of less than 5 mm. Hg, chiefly during the early period of diastole.

TABLE V. AMERICAN HEART ASSOCIATION CLASSIFICATION

	CLASS I	CLASS II	CLASS III	CLASS IV	TOTAL
Number of Cases	0	19 (47.5%)	16 (40%)	5 (12.5%)	40

TABLE VI. DEGREE OF LEFT ATRIAL OPACIFICATION IN 15 PATIENTS STUDIED BY LEFT VENTRICULOGRAPHY

	GRADE I	GRADE II	GRADE III	GRADE IV
Number of Cases	0	3 (20%)	9 (60%)	3 (20%)

TABLE VII. OPERATIVE MORTALITY AND CAUSES OF DEATH

CAUSES OF DEATH	NUMBER OF CASES	PER CENT
Ventricular fibrillation, cardiac arrest, and shock	8	20
Pulmonary edema	1	2.5
Infringement of coronary artery	2	5
Pseudomonas septicemia	3	7.5
Staph. subacute bacterial endocarditis	1	2.5
Total	15	37.5

TABLE VIII. PRE- AND POSTOPERATIVE AMERICAN HEART ASSOCIATION CLASSIFICATION

A.H.A. CLASSIFICATION	PREOPERATIVELY	POSTOPERATIVELY
Class I	0	7
Class II	11	9
Class III	8	3
Class IV	1	1

TABLE IX. EFFECT OF ANNULUS PLICATION ON CLINICAL MANIFESTATIONS

	PRESENT PREOPERATIVELY	POSTOPERATIVE STATUS			
		ABSENT	IMPROVED	SAME	WORSE
Fatigue	18	6	7	5	1
Dyspnea	18	8	5	4	1
PND	9	6	2	0	1
Edema	11	5	3	2	1

A left cardiac ventriculography (direct transthoracic needle puncture opacification of the left ventricle) was done prior to surgery in 15, according to the technique of Lehman.[5] Radiopaque dye was injected rapidly under manometric and electrocardiographic control into the left ventricle, and films were taken at rapid intervals. The degree of left atrial opacification (Table VI) was used to quantitate the amount of mitral regurgitation. It was at least 2 to 4 plus in all patients, based on a range of 0 to 4 plus. The accuracy of this method has been documented in a study of 42 patients with isolated mitral valve disease in whom careful palpation of the mitral valve was subsequently carried out at surgery.[6] Each of the cases with advanced mitral regurgitation had a 2-plus, or greater, opacification of the left atrium on preoperative cardiac ventriculography.

OPERATIVE EVALUATION

Of the 40 patients operated, 11 (27.5%) succumbed at the time of surgery. An additional 4 died during the period of hospitalization which immediately followed. The over-all mortality rate, therefore, was 37.5% (Table VII). The follow-up review included 21 of the 25 patients who survived (Tables VIII, IX, X, and XI). Of these, 1 died as the result of hepatitis. They were followed from 6 to 18 months after surgery.

TABLE X. PREOPERATIVE AND POSTOPERATIVE AUSCULTATORY FINDINGS

	PREOPERATIVELY	POSTOPERATIVELY
Systolic Murmur		
Grade I	0	2 (10%)
Grade II	1 (5%)	10 (50%)
Grade III	17 (85%)	7 (35%)
Grade IV	2 (10%)	1 (5%)
Pulmonic Second Sound		
Grade I	6 (30%)	8 (40%)
Grade II	10 (50%)	12 (60%)
Grade III	4 (20%)	0
Grade IV	0	0
M_1		
Sharp	7 (35%)	3 (15%)
Normal or diminished	13 (65%)	17 (85%)
Diastolic Murmur		
Present	10 (50%)	5 (25%)
Absent	10 (50%)	15 (75%)

TABLE XI. PREOPERATIVE AND POSTOPERATIVE RADIOGRAPHIC CHANGES

	SIZE OF HEART		LEFT AURICLE		PULMONARY ARTERY SEGMENT	
	PREOP.	POSTOP.	PREOP.	POSTOP.	PREOP.	POSTOP.
Absent	0	0	0	1	0	0
Grade I	2	2	3	3	7	8
Grade II	10	10	11	9	10	9
Grade III	6	5	4	5	3	3
Grade IV	2	3	2	2	0	0

1. *Postoperative Clinical Manifestations.*—Improvement in fatigue and dyspnea was noted in 68 per cent and 74 per cent, respectively, of those who recorded these complaints prior to surgery. The results in those who had experienced edema were about the same.

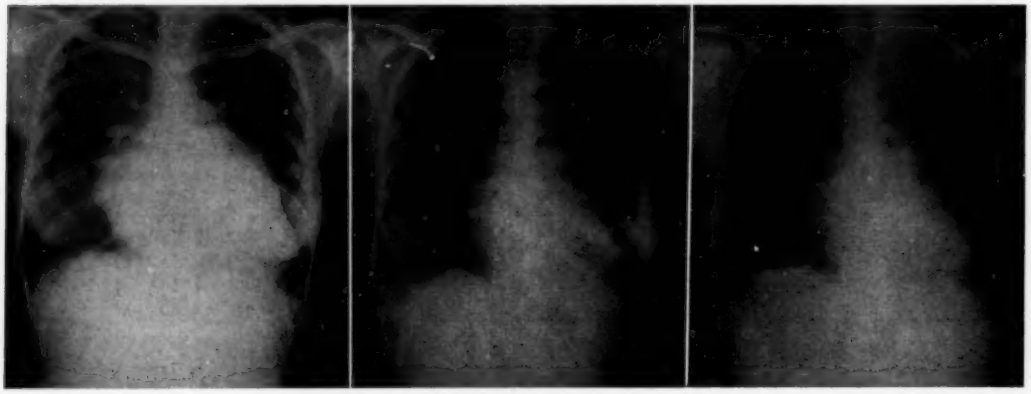
Immediately after surgery the apical systolic murmur was generally less intense. However, in many instances it returned to its initial loudness within 3 months. Nevertheless, as a total experience a murmur of Grade 3 intensity or more was heard in 40 per cent of those in whom it was observed preoperatively.

Although an occasional patient showed striking changes in heart size (Fig. 3), this was not the general rule.

Little change was observed in the electrocardiographic patterns following cross-polar plication.

2. *Special Studies.*—Significant alterations were not noted in the contour of the left atrial curves or in the details of the postoperative left heart catheterizations. In no instance did the catheterization reveal that the operation had produced dynamic mitral stenosis.

Four of the 5 patients in whom a left ventriculogram was performed showed a dramatic decrease in the degree of left atrial opacification (Fig. 4).



A. *B.* *C.*

Fig. 3.—Posteroanterior chest film taken (*A*) prior to cross-polar plication, (*B*) 20 days postoperatively, and (*C*) 1 year after surgery. The greatest diminution in heart size was demonstrated immediately after the annuloplasty.

DISCUSSION

In mitral insufficiency, pathologic physiology develops when the regurgitant stream is of sufficient magnitude to augment the volume load of the left atrium. Under these circumstances the chamber dilates and promotes its output to the left ventricle. The latter also dilates and hypertrophies in response to the newly acquired volume and pressure loads, and an effective output into the aorta may be restored. However, as the left ventricle enlarges, it increases the dilatation of the mitral annulus and thereby aggravates the degree of insufficiency. In brief, incompetence of the mitral valve is a significant defect which may lead to a series of interrelated, self-perpetuating, dynamic events ultimately terminating in left ventricular failure (Fig. 5). The potential and actual seriousness of the lesion explains the continuing interest in its surgical correction.

An evaluation of cross-polar plication requires an examination of the immediate mortality rate and of the physiologic and clinical responses in those who have survived the procedure.

The present mortality rate of 37.5 per cent is considerably higher than that encountered in surgery for mitral stenosis. However, there is reason to believe it can be reduced materially. Two of the patients succumbed as a result of technical errors when coronary arteries were compromised by the suture. Four patients died from resistant septicemia after surgery was successfully concluded. These may have represented superinfection, and similar occurrences should be avoidable with an adjusted antibiotic routine. The elimination of these cases reduces the over-all death rate to a more acceptable 22.5 per cent.

The most frequent cause of death was ventricular fibrillation or cardiac arrest at the time of surgery. The likelihood of this catastrophe or of left ventricular failure increased with the age of the patient, the heart size, and the degree of functional incapacity. All of the patients over 50 years of age died, as compared to 32 per cent of those who were younger; 65 per cent of those with a heart size of Grade III or more succumbed in contrast to 15 per cent with smaller hearts; and 60 per cent of the patients in functional Classes III or IV died, as compared to 20 per cent who were less disabled.

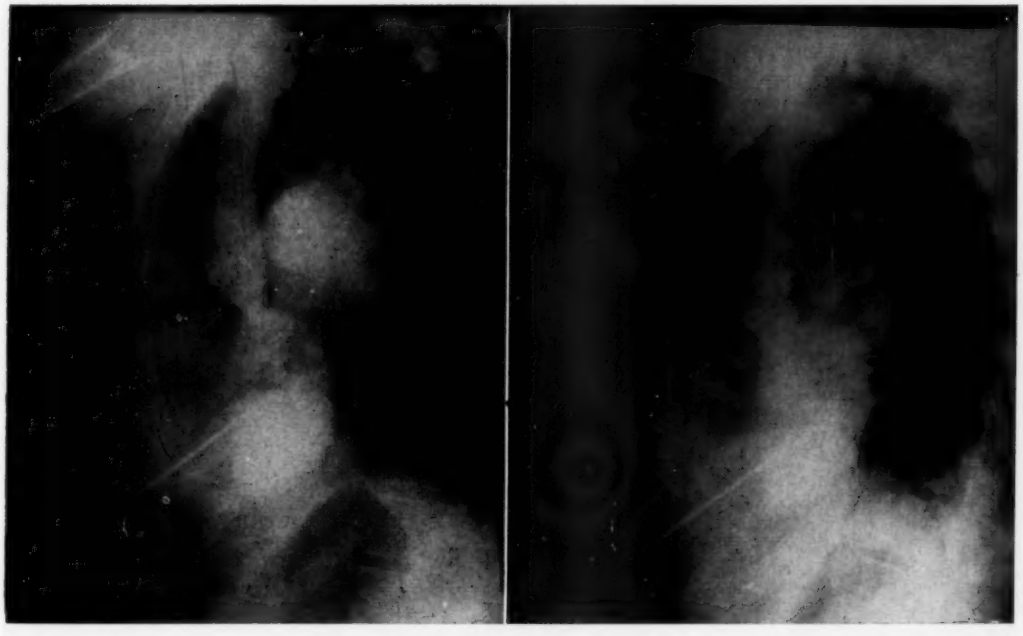


Fig. 4,*A*.

Fig. 4.—Left cardiac ventriculography. A study of patients M.S. (*A*), J.A. (*B*), and H.R. (*C*), before and after cross-polar plication. Injection of radiopaque dye into the left ventricle preoperatively results in immediate reflux opacification of the left atrium. Note changes following mitral annuloplasty in these 3 cases. (For *B* and *C*, see page 272.)

A simple truism is apparent. Cross-polar plication is better tolerated when patients are in the earlier devolutionary stages of their disease. It is accompanied by extreme risks when the heart is unusually large or when functional abilities have been reduced seriously.

Symptomatic improvement was recorded in the vast majority of those who survived surgery. It is pertinent to observe that this improvement was noted

even in those patients who had deteriorated to a Class III functional classification prior to surgery. However, symptomatic benefit was not recorded in the 2 patients who were in the Class IV classification. Hence, it is apparent that an operation which is successful from a technical standpoint, in patients who are

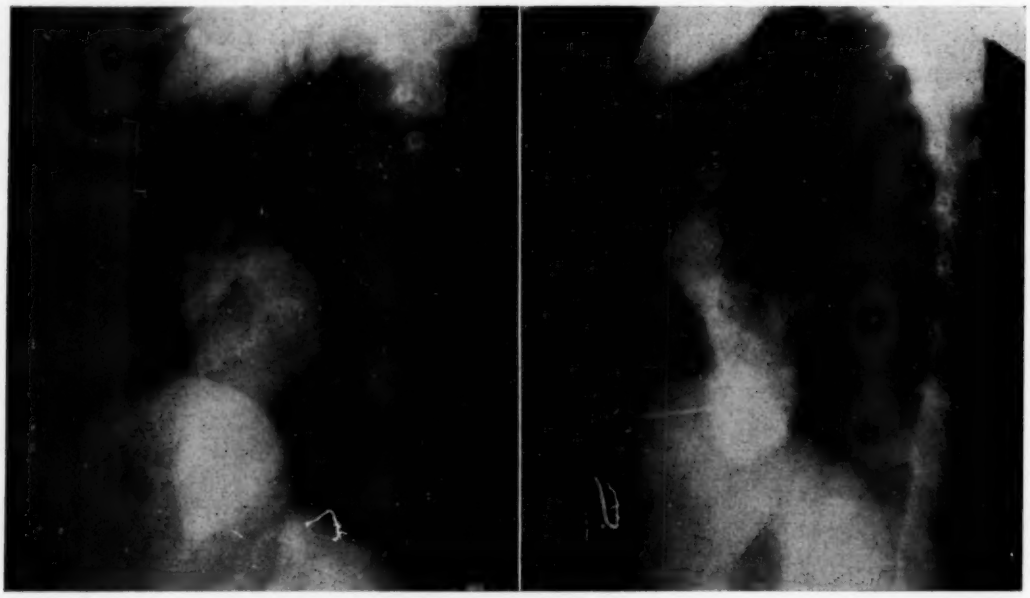


Fig. 4,*B*.—(*For legend see page 271.*)

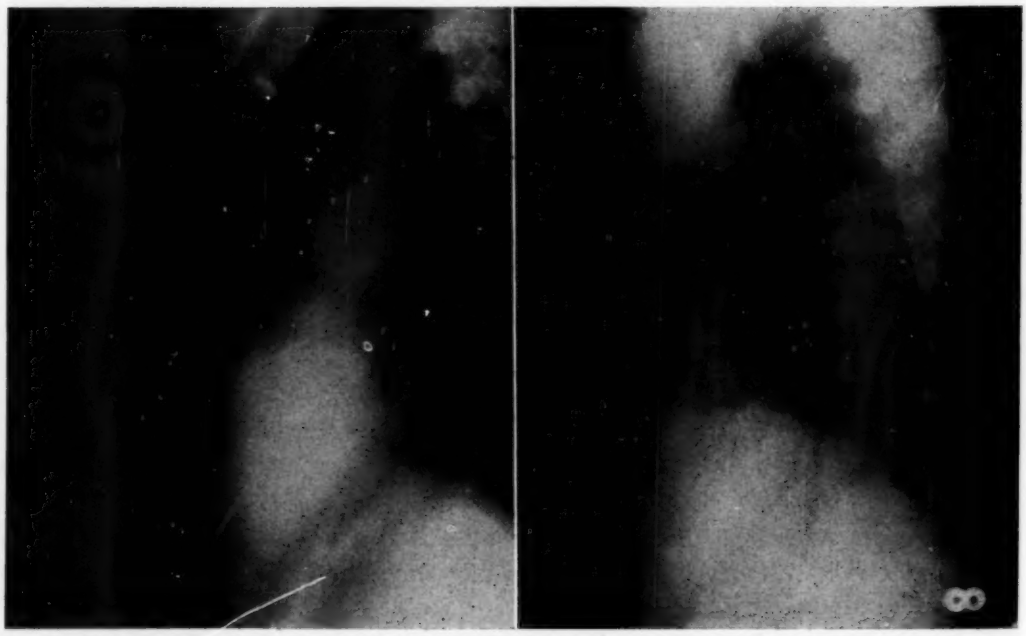


Fig. 4,*C*.—(*For legend see page 271.*)

in the most advanced stages of their disease, may not be accompanied by an amelioration of subjective complaints.

Objective evidence of benefit following cross-polar plication was limited to alterations in the intensity and duration of the apical systolic murmur and changes in the speed and degree of left atrial opacification at the time of left ventriculography.

The frequency and consistency with which the characteristic apical systolic murmur was changed suggests that the surgery was successful in diminishing the magnitude of the regurgitant stream. However, there was a tendency for the murmur to reappear within 3 months. Accordingly, the possibility that the preoperative mitral insufficiency may recur must be acknowledged.

The most accurate objective appraisal of the effectiveness of cross-polar plication was obtained at the time of left ventriculography. In only one instance in which the study was done pre- and postoperatively did the ventriculography fail to reveal a reduction in the intensity of left atrial opacification. It is interesting to note that this patient proved to be a poor result clinically.

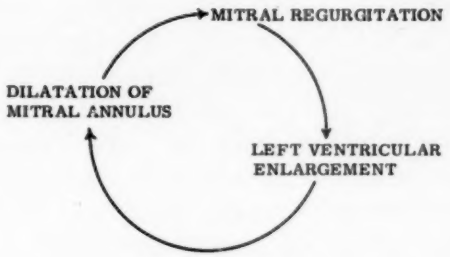


Fig. 5.—The common effects of mitral regurgitation.

SUMMARY

In summary, it is suggested, on the basis of current experiences, that cross-polar plication is an effective method of reducing the circumference of the annulus and, hence, of decreasing the magnitude of the anatomic defect responsible for mitral valve insufficiency. The technique is adequate even under those circumstances in which the incompetence of the mitral valve is due to destruction of leaflet tissue. In these latter instances a reduction in the circumference of the annulus increases the likelihood that the fibrotic or shrunken cusps may more nearly coapt.

The operation is accompanied by a high mortality rate, but most particularly when the patient is in the advanced state of clinical deterioration. It is best tolerated and offers the greatest promise of benefit in those patients in whom the lesion is only moderately advanced.

As in other surgical procedures for acquired heart disease the frequency and consistency of objective improvement is not as significant as the changes in the subjective complaints. Perhaps more distrubing, however, is the possibility that the gains obtained from successfully completed surgery are not always maintained over a long period of time. Despite these failings there is an indication that

cross-polar plication has some merit in the correction of mitral valve incompetence. For the present it appears to be more indicated for patients with moderate disease rather than for those with severe to terminal illness.

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Complete Right Bundle Branch Block Following Cardiac Surgery: Report of Two Cases Persisting After Pulmonary Valvulotomy and Infundibulectomy

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Although numerous articles have appeared in the literature describing the occurrence of bundle branch block in relation to various diseases, congenital cardiac defects, myocardial infarction, and cardiac catheterization, little has been written concerning this conduction defect and its relation to cardiac surgery. Recently, reviewing a series of 26 patients from this clinic who had been operated on for pulmonary stenosis, we have had occasion to review the literature pertaining to such surgery and its results, and find very little mention of this electrocardiographic complication. In view of the greatly increased amount of cardiac surgery being performed at present, it was felt to be of sufficient interest to report on two of our patients in whom complete right bundle branch block (RBBB) developed and persisted following surgery, and to discuss the etiology and physiologic significance of postoperative RBBB.

CASE REPORTS

CASE 1.—A 14-year-old boy underwent a transventricular pulmonary valvulotomy according to the technique of Brock, for relief of an isolated valvular stenosis in 1956. Right ventricular

TABLE I. SUMMARY OF ELECTROCARDIOGRAPHIC DATA

CASE	QRS DURATION (SEC.)		V.A.T. IN LEAD V_1 (SEC.)		ELECTRICAL AXIS (DEGREES)		R.V.P. (MM. Hg)	
	PREOP.	POSTOP.	PREOP.	POSTOP.	PREOP.	POSTOP.	PREOP.	POSTOP.
1	0.06	0.14	0.02	0.09	+95	+112	85	61
2	0.08	0.12	0.05	0.09	+112	+93	133	25

V.A.T. = Ventricular activation time. R.V.P. = Right ventricular systolic pressure.

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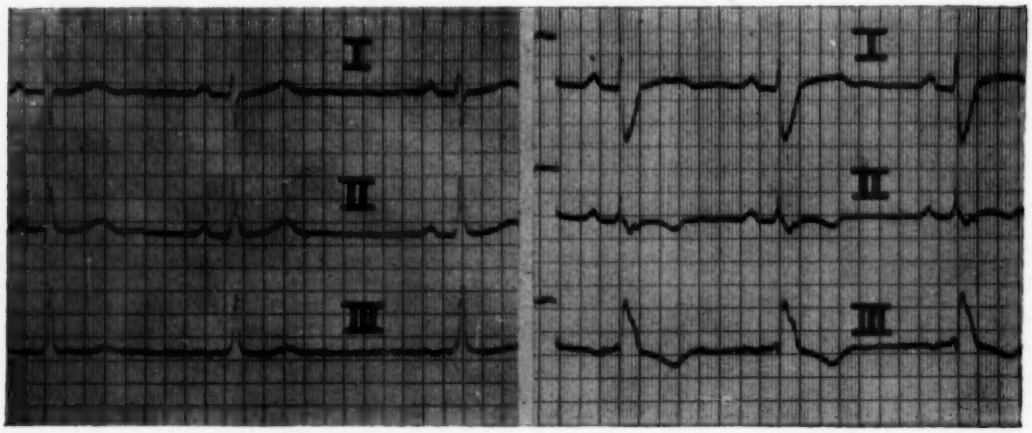
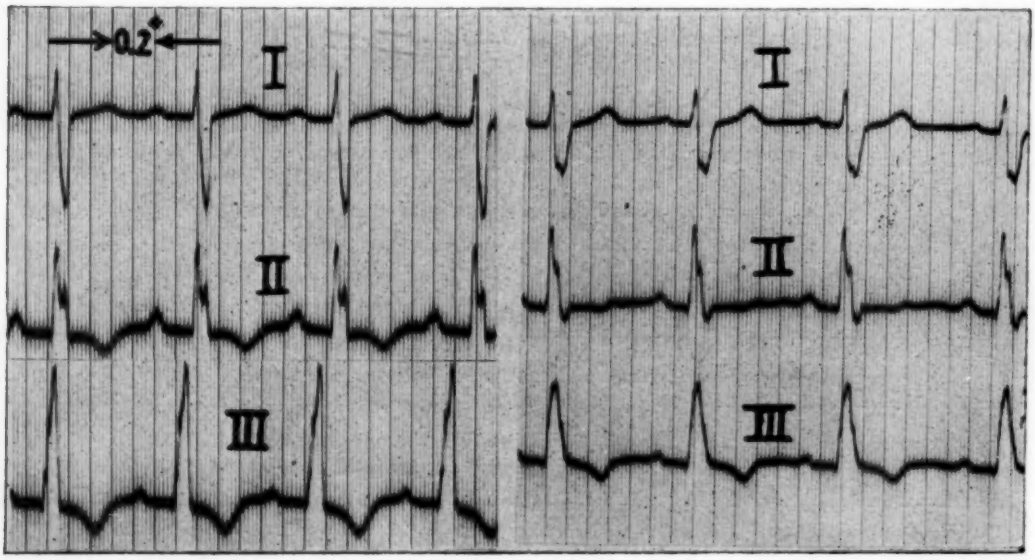
systolic pressure prior to surgery was 85 mm. Hg. Although a poor operative result was achieved, the pressure being lowered to 61 mm. Hg, a good clinical response was seen. Preoperative electrocardiograms had shown no evidence of right ventricular hypertrophy and a normal right axis deviation (Table I). The QRS interval was 0.06 second. On the day following surgery an ECG showed development of complete RBBB with a QRS interval of 0.14 second (Fig. 1). This has now persisted for 15 months.

CASE 2.—A 17-year-old boy was operated on in 1956, for an isolated infundibular pulmonary stenosis, the procedure consisting of "open" infundibulectomy under hypothermia and artificial circulation. Preoperative right ventricular pressure was 133 mm. Hg. An excellent operative



A. *B.*

Fig. 1.—Case 1. Leads I, II, and III. *A*, Preoperatively. QRS = 0.06 sec.; electrical axis +95 degrees. *B*, Following surgery. QRS = 0.14 sec.; electrical axis +112 degrees. Time intervals of tracings are 0.10 sec. between heavy lines.



A. *B.*

Fig. 2.—Case 2. Leads I, II, III. *A*, Prior to surgery. QRS = 0.08 sec.; electrical axis +112 degrees. *B*, Postoperatively. QRS = 0.12 sec.; electrical axis +93 degrees. Time intervals are the same as in Fig. 1.

result was obtained, and recatheterization 12 months later showed that the pressure had dropped to 25 mm. Hg. The patient's clinical response has also been good, resumption of completely normal activity being possible.

Electrocardiograms preoperatively showed right ventricular hypertrophy, abnormal right axis deviation, and a QRS interval of 0.08 second. Immediately postoperatively the pattern of complete RBBB with a QRS interval of 0.12 second was seen. Follow-up studies have shown this block to be persisting 12 months after surgery (Fig. 2).

DISCUSSION

Electrocardiographic abnormalities are a frequent finding in congenital heart disease and during catheterization and surgery in patients with such defects. It is well known that various degrees of heart block, A-V dissociation, auricular and ventricular tachycardia, and auricular fibrillation all occur during these diagnostic and corrective procedures, but they are largely of a transient nature and without any known lasting physiologic significance. In the only articles since 1950, which could be found[1,2] describing persistent postoperative ECG abnormalities, Kittle[1] reports on 4 cases of RBBB, and Fry[2] on one complete A-V block following surgery for relief of pulmonary stenosis. The general literature pertaining to results of such surgery,[3-8] including our own 26 cases, produces a total of 348 patients in whom specific information is given regarding pre- and postoperative electrocardiograms. From a total of 92 transventricularly operated cases, Campbell and Brock[4] mention "one case of RBBB," but do not say whether it was of the complete type or whether temporary or permanent in nature. Lillehei,[6] in 43 patients operated by the transventricular approach, reported one complete RBBB persisting for an unstated period. The reported incidence of occurrence of this conduction defect is thus 8 in 348 operations, or slightly over 2 per cent; 5 of the blocks developed following valvulotomy and 3 after infundibular resection. This figure is in reality undoubtedly too high, however, when one considers that well over 600 valvulotomies and infundibulectomies for "isolated" stenosis have been reported, and that in many of these reports little or no mention is made of electrocardiographic data. It is interesting to note that all of the bundle branch blocks complicating valvulotomy occurred following a transventricular approach to the valve; none developed after transarterial surgery, either with the valves under direct vision or according to Söndergaard's method. On the other hand, those blocks associated with infundibular resection appeared following both "blind" and "direct-vision" operations. This leads us to a discussion of the possible etiology of the block in these cases.

Perhaps the first assumption to be made in explaining the etiology of postoperative RBBB would be that direct surgical manipulation had disturbed the conduction pathways. Since the proximal third of the right bundle proceeds from the A-V node, in a position immediately beneath the endocardium, to the region of the crista supraventricularis, its vulnerability is great. Damage to the bundle is easily conceivable in this region when a valvulotome or dilator is pushed through a small ventricular opening without benefit of direct vision.

Were the development of RBBB due to a short, surgically induced strain beyond a critical point in an already overloaded and anoxic myocardium (which

is very improbable in our first case), it is not unreasonable to expect that such a block would soon regress following myocardial healing and return of intracardiac hemodynamics to a more normal status. We are therefore in agreement with Kittle that the operative procedure per se, apart from the valvular or infundibular manipulation, is not a likely etiological factor.

As long as there are no large postoperative residual strains on the heart, such as marked right ventricular hypertension, anoxia, or other associated congenital defects, we believe that the conduction defect is in itself of minimal importance. It is well known that persistent RBBB, occurring after diphtheria and other acute illnesses, has quite a good prognosis, being the result of a single, isolated injury. It seems reasonable that operatively induced block, whatever the true specific cause, would more closely approximate this type. Conversely, those blocks associated with hypertension, myocardial infarction, and conditions causing prolonged and chronic cardiac strain, present quite a different picture, their development often signalling a critical turning point in the course of the basic disease. Complete RBBB has been observed in 6 other cases of congenital heart disease from this clinic; these patients have not had any cardiac surgery, and without exception all had malformations consistent with prolonged and severe intracardiac hypertension. The supposition of relative unimportance of the postoperative RBBB in the two cases presented here is in agreement with the observations in Kittle's patients in which no untoward effects of the conduction defect on the patients' condition could be detected. Complete RBBB following pulmonary valve or infundibulum surgery, therefore, does not appear to be a serious complication if the surgery itself has been successful and no residual cardiac defect producing strain exists.

SUMMARY

1. Two cases of complete right bundle branch block persisting after pulmonary valvulotomy and infundibulectomy are presented. The electrocardiographic abnormality has persisted for 15 and 12 months, respectively.

2. The incidence of postoperative RBBB is calculated to be very low, following a review of the reported operative series.

3. Etiology of the defect is suggested to be direct trauma to the right conduction bundle rather than other factors which could not account for the block's apparently irreversible nature.

4. No definite physiologic significance can be attached at present to development of such a bundle branch block, providing no other cardiac abnormality exists in conjunction with it.

ADDENDUM

Since preparation of this report, two further cases of complete RBBB have been seen following cardiac surgery in this clinic. One patient, a 9-year-old girl, underwent closure of a ventricular septal defect via suturing of a plastic sponge prosthesis, as well as a resection of the crista supraventricularis for infundibular pulmonary stenosis. A QRS prolongation of 0.11 to 0.12 second has now persisted for 2 months postoperatively. The other case, a 20-year-old man, was submitted to resection of the crista supraventricularis for an infundibular stenosis. One month

postoperatively the ECG still shows complete RBBB with a QRS interval of 0.12 to 0.14 second. Both of these operations were performed under direct-vision, "open-heart" surgery, using a heart-lung machine.

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The Racial Incidence of Heart Disease at Groote Schuur Hospital, Cape Town. Part I. Coronary Vascular Disease

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The etiology of coronary vascular disease, by which is meant coronary atheroma and coronary thrombosis, is as yet unknown. Of the many factors implicated, geographic and climatic environment cannot in any way be responsible. Thus, in Cape Town we have a multiracial community living in the same climate, with each race, in the main, adhering to its own traditional customs, particularly as regards diet,[1] and yet the incidence of coronary vascular disease differs remarkably in each group.

In a preliminary report, Vogelpoel and Schrire[2] found the incidence of cardiac infarction to be far higher in the White population than in the Cape Colored, whereas the disease was practically nonexistent in the Bantu. It is the purpose of this paper to extend and expand this study and to confirm the differing racial incidence of coronary vascular disease in Cape Town.

Of the three racial groups, the Whites are mainly descendants of immigrants from Great Britain and Holland and are economically privileged. Their number has gradually increased by natural rise in births, by drift from the country to the city, and by immigration from Europe. Even the patients who attend the public hospital (Groote Schuur Hospital), although representing the poorer section of the White community, earn considerably more than the Non-White population.

The Cape Colored community originated mainly from European, Hottentot, and Malay stock, the Hottentot comprising the original indigenous population of the Cape. Only within the last few decades has any Bantu been added. Included in this group is a section of Cape Malays (of Moslem faith), who are said to be relatively pure descendants of imported Malays. From the socioeconomic point of view the Cape Colored population are intermediate between the Whites and the Bantu. They compete in the skilled and unskilled labor market, and,

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compared with the Bantu, have a far greater proportion of professional men, although, of course, far fewer than the Whites.[1] Like the Whites, they are relatively stable and migrate rarely. They have increased considerably in numbers both by natural increase in birth rate, which is higher than that of the Whites, and by drift from the country to the city.

The Bantu, as a rule, are lowest in the socioeconomic scale, providing the unskilled and heavy manual labor. Migrating often from the rural areas, their stay in the city is temporary, from one-half to two years, during which time they attempt to save money to meet their own needs and the needs of their homes in the Reserves. However, there are some who have lived most of their lives in the city or have been born there. These approach closest to the Whites in education, employment, and diet. Few, however, have as yet reached the professional class. Their numbers have tended to fluctuate and they have been actively encouraged to return to the Reserves. Their birth rate is high but the immigration of their womenfolk is definitely discouraged.

Groote Schuur Hospital was the main hospital serving the population of Cape Town and the surrounding districts during the five years under review, namely, 1952 to 1956. It is an 854-bed hospital, with slightly more White beds than Non-White, and serves as the main teaching hospital of the Faculty of Medicine of the University of Cape Town. During 1955 and 1956, however, the 44 teaching beds of the New Somerset Hospital, which serves the Non-White population only, was included in this study, thus making the White and Non-White bed state approximately equal.

The hospital population is selected because a means test prevents the attendance of the wealthier section of the population. Almost all the Non-Whites are eligible and this includes probably all the Bantu.

It has been generally accepted that coronary vascular disease occurs in the more privileged section of a community where the factor of multiple racial groups is not operative.[3-7] An attempt was made, therefore, to determine the incidence of this condition in the wealthier Whites who were excluded from the hospital. Physicians on the staff of Groote Schuur Hospital who were also in private practice were asked to record their experience among Whites during 1955 and 1956. Accurate figures were not available, but the uniform impression was that the incidence of this disease was greater outside than inside the hospital. It would appear, therefore, that the data emerging from this study underestimate the incidence of coronary vascular disease in the total White population of Cape Town, but provide a more accurate indication of the incidence in the Cape Colored and Bantu populations.

MATERIAL AND METHODS

During the period under survey the electrocardiographic service of the Cardiac Clinic included all inpatients and outpatients attending Groote Schuur Hospital, and the 44 inpatient teaching beds of the New Somerset Hospital. Inasmuch as over 99 per cent of the 21,582 records were interpreted by the author, any errors in electrocardiographic interpretation were constant in all racial groups. The same physicians and surgeons see patients of all races and the facilities for obtaining electrocardiographic investigation are equal. The data obtained, therefore, reflect the relative incidence of the disease as it occurs in this hospital.

Official figures compiled by the Bureau of Census and Statistics in 1951, reveal that the population of Cape Town consisted of 247,442 Whites, 272,314 Cape Colored, and 49,793 Bantu, whereas in March, 1957, there were 280,000, 351,100, and 67,800, respectively. Whereas the White and Cape Colored include the total population of a relatively stable people, probably half the Bantu are migrant laborers between the ages of 20 and 40. Moreover, an accurate census of the Bantu is not possible, and it is felt generally that the number of Bantu is definitely underestimated by the official figures.

During the years 1952 through 1956, the number of patients attending General Out-Patients at Groote Schuur Hospital was 1,511,336. This figure includes all attendances and does not refer to individual patients. During the same period, 107,943 patients were admitted to the wards. The proportion of White to Cape Colored and Bantu patients is shown in Table I.

TABLE I. ATTENDANCE OF WHITE, CAPE COLORED, AND BANTU PATIENTS AT GROOTE SCHUUR HOSPITAL DURING 1952-1956

YEAR	WHITE	CAPE COLORED	BANTU
	Outpatients		
1952	147,299	137,844	25,829
1953	154,860	146,556	26,101
1954	122,065	131,981	21,419
1955	129,889	140,008	22,402
1956	135,889	144,047	25,147
Total	690,002	700,436	120,898
	Inpatients		
1952	9,646	8,316	1,770
1953	10,036	9,211	1,810
1954	10,656	9,326	1,789
1955	10,875	9,432	1,893
1956	10,976	10,140	2,067
Total	52,189	46,425	9,329

Thus, the attendance of Whites and Cape Colored at General Out-Patients is approximately equal. If we add the Cape Colored patients from the New Somerset Hospital to those from Groote Schuur Hospital, then the admissions to In-Patients are also approximately equal. The Bantu subjects, even though significantly fewer than either of the other two groups, were well represented in the hospital population, although it must be remembered that the older age group was probably poorly represented compared with the other two groups.

Rigid criteria were used in the diagnosis of myocardial infarction. Abnormal T-wave and S-T-segment changes alone were not accepted. As previously described[2] in anterior infarction, wide or deep Q waves in the precordial leads (V_1-V_7) or diminution in the R waves across the precordium with T-wave inversion or S-T-segment change were required. In posterior infarction a Q wave of at least 0.04 second in width, or deeper than 30 per cent of the R wave in aV_F, was accepted. In the presence of right bundle branch block a Q wave of 0.04 second in aV_F or abnormally wide Q waves in the precordial leads indicated infarction. Infarction was very seldom diagnosed in the presence of left bundle branch block, unless Q waves or definite S-T-segment depression over the left ventricle were present.

To test the validity of these electrocardiographic criteria, 581 case histories of patients showing cardiac infarction as assessed by these electrocardiographic criteria were selected for study.[8]

The detailed history, physical findings, and special investigations were analyzed, and in many cases post-mortem proof was obtained. Over 100 patients were reassessed and re-examined in the Cardiac Clinic. Two hundred and thirty-nine patients were on long-term anticoagulant therapy or had received short-term anticoagulant therapy with the clinical diagnosis of cardiac infarction, and were on the files of the anticoagulant service of the hospital. Of the 581 cases only 22 (3.7 per cent) were discarded. In 8 cases the diagnosis of anterior infarction had been confused with marked right ventricular dilatation with loss, or diminution, of R waves in the anterior chest leads. Most of the remaining 14 cases were discarded in the absence of any history suggestive of infarction, although the presence of hypertension, diabetes, or arteriosclerosis made the association very likely.

If, however, less rigid electrocardiographic criteria[9] were adopted, a further 792 cases could be accepted for analysis. In these cases T-wave inversion without Q waves over the anterolateral or posterior aspects of the left ventricle, or bundle branch block without significant Q waves or S-T-segment shift, were present. A history of angina pectoris or cardiac infarction was demanded in addition, for it was found that the electrocardiographic changes were not sufficiently distinctive for the diagnosis. Thus, in an analysis of 256 cases showing T- or ST-T-wave change only, in the same way as described above, the diagnosis was found to be acceptable in only 192. The greatest difficulty was experienced in differentiating the changes of left ventricular hypertrophy from those of ischemia, particularly when the two conditions coexisted. Similarly, the presence of bundle branch block was frequently found in the absence of a history suggestive of coronary vascular disease. Thus, 24 of 56 cases of bundle branch block chosen at random for study had no history of angina pectoris or cardiac infarction.

Patients with normal graphs were not considered in this analysis. Whereas a normal resting graph is not rare in coronary vascular disease, particularly in angina pectoris, the margin of error was too great. Of 58 cases chosen at random 19 were found to be unacceptable, the diagnosis on the electrocardiogram request form being unreliable in these cases.

RESULTS

During the five-year period 1952 through 1956, there were 12,512 patients over the age of 12 years. The ratio of White to Cape Colored to Bantu patients was 9.2:5.7:1 (Tables II and III).

If only patients over the age of 30 were considered, the racial distribution of electrocardiograms in the Whites, Cape Colored, and Bantu was 10:5.6:1 (10,478 patients), that is, approximately the same as in those over the age of 12.

Of the 12,512 patients, 991 showed the classical pattern of myocardial infarction. Of these, 760 (76.6 per cent) were in Whites and 228 (23.1 per cent) in Cape Colored (Table II). There were 3 Bantu cases (0.3 per cent).

TABLE II. RACIAL INCIDENCE OF MYOCARDIAL INFARCTION DETERMINED ELECTROCARDIOGRAPHICALLY (RIGID CRITERIA) IN ADULTS OVER THE AGE OF 12

RACE	RACIAL DISTRIBUTION OF ELECTROCARDIOGRAMS		RACIAL DISTRIBUTION OF INFARCT PATTERNS		PERCENTAGE OF RACES IN 991 INFARCTS	PERCENTAGE OF ELECTROCARDIOGRAMS SHOWING INFARCTS
	NUMBER	RATIO	NUMBER	RATIO		
White	7,232	9.2	760	253	76.6	10.5
Colored	4,497	5.7	228	76	23.1	5
Bantu	783	1	3	1	0.3	0.4
Total	12,512		991			

TABLE III. RACIAL INCIDENCE OF "CORONARY VASCULAR DISEASE" DETERMINED ELECTROCARDIOGRAPHICALLY IN ADULTS OVER THE AGE OF 12

RACE	RACIAL DISTRIBUTION OF ELECTROCARDIOGRAMS		RACIAL DISTRIBUTION OF ABNORMAL PATTERNS		PERCENTAGE OF RACES IN 1,783 CASES	PERCENTAGE OF ELECTROCARDIOGRAMS SHOWING INFARCTS
	NUMBER	RATIO	NUMBER	RATIO		
White	7,232	9.2	1,349	270	75.6	18.7
Colored	4,497	5.7	429	86	24.1	9.5
Bantu	783	1	5	1	0.3	0.6
Total	12,512		1,783		100	

TABLE IV. DISTRIBUTION OF CORONARY DISEASE BY DECADE FROM 20 TO 60 YEARS AND OVER IN WHITES, CAPE COLORED, AND BANTU

AGE	WHITE			CAPE COLORED			BANTU		
	NUMBER	PER CENT	TOTAL ECGS	NUMBER	PER CENT	TOTAL ECGS	NUMBER	PER CENT	TOTAL ECGS
20–29	8	0.6	409	7	1.6	578			111
30–39	53	3.9	578	22	5.1	641	3	60	141
40–49	213	15.5	1,277	119	27.7	933	1	20	162
50–59	404	30	1,676	144	33.6	1,030			213
60+	671	50	2,898	137	32	890	1	20	109
Total	1,349	100	6,838	429	100	4,072	5	100	736

TABLE V. SEX DISTRIBUTION OF CARDIAC INFARCTION (IN DECADES) IN 991 CASES IN WHITES, CAPE COLORED, AND BANTU

AGE	WHITE			CAPE COLORED			BANTU		
	MALE	FEMALE	M/F RATIO	MALE	FEMALE	M/F RATIO	MALE	FEMALE	TOTAL
Under 30	2	1	2:1	5	0				8
30–39	22	5	4:1	12	3	4:1	2	0	44
40–49	110	18	6:1	51	12	4:1			192
50–59	181	62	3:1	58	13	4:1			314
60–69	134	80	1.7:1	43	11	4:1	1	0	268
70+	95	50	2:1	12	8	1.5:1			165
Total	544	216	2.5:1	181	47	4:1	3	0	991

Of the 792 cases with a history of angina pectoris or cardiac infarction with an abnormal electrocardiogram ("coronary vascular disease"), there were 589 Whites, 201 Cape Colored, and 2 Bantu. The total number of electrocardiograms showing evidence of "coronary vascular disease," therefore, was 1,783, of which 1,349 were found in White, 429 in Cape Colored, and 5 in Bantu patients (Table III). Of the latter 5, one was a visitor from the Belgian Congo.

Effect of Age.—The distribution of coronary disease by decade from 20 years and over in the three racial groups is shown in Table IV. A detailed knowledge of the age distribution of the population attending the hospital could not be obtained.

Effect of Sex.—The effect of sex on the incidence of coronary vascular disease is shown in Table V (rigid criteria) and in Table VI (over-all figures).

TABLE VI. SEX DISTRIBUTION OF CORONARY VASCULAR DISEASE (IN DECADES) IN 1,783 CASES IN WHITES, CAPE COLORED, AND BANTU

AGE	WHITE			CAPE COLORED			BANTU		
	MALE	FEMALE	M/F RATIO	MALE	FEMALE	M/F RATIO	MALE	FEMALE	TOTAL
Under 30	5	3	1.6:1	7	0				15
30–39	42	11	4:1	16	6	3:1	3	0	77
40–49	167	46	4:1	78	41	2:1	1	0	334
50–59	263	141	2:1	96	48	2:1			548
60–69	218	173	1.2:1	71	32	2:1	1	0	495
70+	165	115	1.5:1	18	16	1.1:1			314
Total	860	489	1.8:1	286	143	2:1	5		1,783

DISCUSSION

Almost twice as many electrocardiograms were requested for White as for Cape Colored patients (7,232:4,497), although the hospital and general population was approximately equal. This suggests that attention is drawn to the heart more often in the White than in the Cape Colored patients, and the chief reason for this is the greater incidence of coronary vascular disease in the Whites.

If we analyze the data obtained by using strict electrocardiographic criteria for infarction, three times as many cases occur in the Whites as in the Cape Colored (760:225). That the criteria used were valid was borne out by a thorough review of 581 cases showing these patterns. If the criteria used were less rigid, the same ratio was obtained, but naturally the number of cases analyzed was greater (1,349:426). In the case of the Bantu, the figures are even more striking; thus, ten times as many electrocardiograms were requested for the Whites as for the Bantu, although the White hospital population was only six times that of the Bantu. The incidence of infarction, using strict electrocardiographic criteria, was 253:1 (760:3), and with less rigid criteria it was 270:1 (1,349:5).

If we express the number of cases as a percentage of the total number of electrocardiograms taken in each group (Tables II and III), as in a previous communication,[2] the actual difference is well shown. Thus, a hundred electrocardiograms in Whites included 10.5 infarctions (rigid criteria) or 18.7 (less rigid criteria); one hundred electrocardiograms in Cape Colored showed 5 and 9.5, respectively; and a hundred electrocardiograms in Bantu included 0.4 and 0.6, respectively.

The difference in the incidence of coronary vascular disease in the three racial groups cannot be attributed entirely to an age factor (Table IV). In the absence of detailed knowledge of the nature of the population attending the hospital, however, or of the relative age incidence in the three racial groups attending the hospital, this conclusion is not absolutely valid from the pure statistical point of view, although the inference is highly likely.

Both in Whites and in Cape Colored, over 90 per cent of the cases occurred in patients aged 40 years and older (Table IV). The peak incidence in Whites was between the ages of 50 and 69 years, the maximum number of cases occurring in the decade 50-59. In the Cape Colored the peak decade was similarly 50-59, but more cases occurred between the ages of 40 and 49 than between 60 and 69 (Table VI).

A similar peak incidence between the ages of 50 and 60 years has been reported by Friedberg[10] and Master and associates,[11] although others[12-14] have found the peak incidence between 60 and 70. There were 4.5 and 6.5 per cent of the cases in Whites and Cape Colored, respectively, under the age of 40. There were 15 cases under the age of 30, the youngest being 9. The incidence of cardiac infarction in the younger age groups has been frequently reported, especially during the Second World War,[15-19] and the subject has been well reviewed by Yater and associates.[19]

The effect of sex on the incidence of infarction is well borne out in Tables V and VI. Thus, in Whites during the reproductive cycle (20-49) the incidence in males is four times that of females, when all the cases are considered, and up to six times when cases showing infarction (rigid criteria) are analyzed. In the Cape Colored the figures are two to one and four to one, respectively. The difference in sex incidence is even more striking in the Bantu. No case has yet been noted in a female Bantu in Groote Schuur Hospital, although the figures are too small to have statistical significance. With advancing age there is a tendency for females to catch up with the males, although at no age in our series have the two sexes been equal. These figures are in accordance with data published elsewhere. Thus, figures from Minnesota[20,21] show a far greater severity of atherosclerosis in men than in women. The severity of coronary sclerosis in women increases steadily from the fourth to the eighth decade, leveling off in the ninth decade.[20] In men, leveling off takes place after the sixth decade. At all ages atherosclerosis is far commoner in men than in women, although this is most marked between the ages of 50 and 59. In Boston,[22] in young adults, men outnumbered women approximately three to one, and in the middle age group by two to one. At the age of 70 and over there was no significant sex difference. Similar results are reported from other centers in the United States.[12,23-28]

The incidence also was found to be higher in the better economic groups. In Britain,[13,29-31] the incidence in men was found similarly to be far higher than in women. The male death rate from cardiac infarction in the age range of 40 to 50 was more than five times greater than for females; from 55 to 60 it dropped to four times, and at age 75 and over to less than two times.[6] The preponderance of males is most striking where there is neither hypertension nor diabetes mellitus present, but these factors were not analyzed in this series.

Keil and McVay,[32] on the other hand, have reported an equal incidence of myocardial infarction in male and female American Negroes. In their series the usual predominance of European (Caucasian) males over females (three to one) was recorded. The incidence of myocardial infarction in the Negro, however, was approximately 52 per cent of that in the Caucasian. (The American Negro would be regarded in Cape Town as Colored and not as Bantu.)

These figures contrast strikingly with our findings in the Bantu. While the incidence of cardiac infarction is extremely uncommon in the Bantu male, it appears to be absent in the Bantu female, although the figures are too small to have statistical significance. Hypertension and diabetes mellitus are encountered in the Bantu male and female,[33] the latter less frequently than in the Whites and Cape Colored. It is well recognized that coronary disease, particularly in the female, is frequently associated with hypertension or diabetes mellitus,[34-39] but clearly the immunity to the development of coronary disease in the Bantu cannot be attributed to immunity from those diseases.

The relative incidence of coronary vascular disease in the three racial groups in Cape Town, at necropsy, has been reported by Schrire and Uys.[40] The Department of Pathology draws its material from the Groote Schuur Hospital. During the years 1952 through 1956, 11 per cent of the necropsies in patients over the age of 10 (188 of 1,651) were on Bantu, and of the remainder, 705 were on Cape Colored and 758 on Whites. Despite this bias of numbers in favor of the Non-Whites, there were 119 cases of cardiac infarction in Whites and 43 in Cape Colored. There were only 2 cases of cardiac infarction in the Bantu in the records of the Pathology Department, and in neither case was there evidence of coronary atheroma. Infarction was associated with malignant hypertension in the one case and with syphilis in the other. There is only one proved case of cardiac infarction on the basis of coronary atheroma, in a Bantu male who died suddenly and was necropsied at the Government Medico-Legal Laboratory.[40]

The data obtained, therefore, is in conformity with the findings elsewhere in Africa. The rarity of coronary thrombosis in the Bantu in Johannesburg has been reported by Becker,[41] Higginson,[42] and Elliott[43]; in Rhodesia by Gelfand[44]; in Uganda by Davies[45] and Williams[46]; and on the Gold Coast by Edington.[47]

It has been suggested that a European diet rich in fats (particularly of animal origin) is implicated in the pathogenesis of coronary atheroma, as it is in the elevation of the blood cholesterol level.[48-58] Bronte-Stewart, Keys and Brock[1] carried out a survey on 600 males between February and May, 1956, in Cape Town. There were 132 Bantu, 118 Cape Colored, and 114 Whites of this group who had their blood cholesterol and serum lipids analyzed. A highly significant difference in the mean total cholesterol level and, particularly, in the

cholesterol level in the beta lipoprotein fraction of the serum was found when the men were classified according to their racial origin. This difference these authors correlated with the large difference between the racial groups as regards their average diets, particularly the habitual consumption of fats. The fat consumption of the Whites is more than twice that of the Bantu, with the Cape Colored intermediate. The authors concluded that the results of their survey supported the hypothesis that the dietary intake of fat influences the level of serum cholesterol, and particularly that of the beta lipoprotein, and inferred that this may be one of the major factors influencing the pathogenesis of coronary heart disease.

The results obtained in this study show that there is a considerable difference in the incidence of coronary vascular disease in the three racial groups. The Whites far outnumber the Bantu, and the Cape Colored fall between the two groups. Whether this is related to the difference in dietary habits of the three racial groups, however, remains to be proved. Yudkin[59] has recently analyzed critically the evidence. That multiple causes are involved appears clear, and this indicates factors such as overconsumption of food, reduced physical exercise, smoking, nervous strain, tension, and type of occupation. Friedman and Rosenman[60] have analyzed the dietary intake of fat in a group of American men and women and reviewed the data relating to the relative immunity of the American woman from coronary vascular disease. Clearly, the factor of sex plays a most important part in the pathogenesis of the disease, and probably this is related to some defect of metabolism in the male. The tremendous importance of sex is borne out by our figures which show a consistently higher occurrence in males of all races. Lastly, the role played by intravascular thrombosis[61-64] in the etiology of atheroma is not yet fully understood. There is as yet no information on the influence of this factor on the incidence of this disease in the three racial groups studied.

In conclusion, it can be stated definitely that a considerable difference in incidence of coronary vascular disease exists in the three racial groups of Cape Town. No difference in the anatomy of the heart and coronary circulation[65] or in blood coagulation has yet been demonstrated. Certain imponderable factors such as stress and strain, emotional and physical, are difficult to assess or measure. A parallel difference in diet, however, particularly the amount of animal fat consumed has also been shown to exist. Whether the two are causally related still remains to be proved.

SUMMARY

1. Twelve thousand five hundred and twelve electrocardiograms of adults (over the age of 12) attending the Groote Schuur Hospital in Cape Town during the years 1952 through 1956 were analyzed to determine the racial incidence of myocardial infarction.

2. Electrocardiographic evidence of coronary vascular disease was very uncommon in the Bantu, occurring in only 3 cases, and in an additional 2 cases there was a history of coronary vascular disease associated with an abnormal tracing.

3. Electrocardiographic evidence of coronary vascular disease was found more commonly in the White than in the Cape Colored population (1,349:426).

4. This disproportionate incidence occurred in all age groups over the age of 30 and was probably not due to a significant difference in age distribution of the population studied.

5. The peak incidence was found between the ages of 50 and 59, with less than 10 per cent below the age of 40.

6. The incidence was far higher in males than in females at all ages, but over the age of 70 the difference was slight. No case was encountered in a Bantu female.

7. The significance of these findings is discussed.

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Wenckebach Periods in Pregnancy and Puerperium

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Second degree atrioventricular block occurs very rarely in the absence of drug intoxication or overt organic heart disease; the Wenckebach period subgroup of second degree block is seen even more rarely. No correlation between this phenomenon and pregnancy or the post-partum state has been reported in the literature. After seeing in consultation several otherwise healthy young post-partum patients with Wenckebach periods demonstrated on electrocardiogram, a study of the incidence and significance of this finding was made.

METHODS AND RESULTS

Twenty-six thousand and ninety-three electrocardiograms taken at the Heart Station of the City of Memphis Hospitals, between 1948 and 1957, have been reviewed; Wenckebach periods were found in 32 patients. Of these patients, 25 had organic heart disease. Twelve patients were female; 13 were male. Only 3 patients were Caucasian, while the remaining 22 were Negroes. This racial preponderance reflects the percentage of Negro admissions to this hospital. It is apparent from the figure that most of these patients were in the later years of life. The salient features of these cases are presented in Table I.

Twenty of the 25 were on digitalis therapy when the Wenckebach periods were demonstrated. Ten patients presented evidence that their conduction defects were probably due to digitalis overdosage; that is, the electrocardiogram showed multifocal ventricular premature contractions, or the Wenckebach periods disappeared either on omission of digitalis or on administration of potassium. One patient was considered to have digitalis overdosage, with no history of such medication, because of her low intelligence, nausea and vomiting, electrocardiogram, and improvement on administration of potassium chloride. In only 4 patients was there neither history nor other evidence of digitalis ingestion. It will be noted from the table that of these 4, only 1 was less than 65 years old; furthermore, all 4 had definite organic heart disease.

The 7 remaining patients with Wenckebach periods but without other evidence of organic heart disease were all under 40 years of age (see Fig. 1). Six were either pregnant or in the puerperium; all were multiparous.

CASE SUMMARIES

CASE 1.—G. B., a 23-year-old Negro woman (Gravida IV, Para III), had the premature delivery of stillborn twins (7 months' gestation) on Sept. 3, 1955, at 2:30 P.M. Her pregnancy was complicated by a mild iron deficiency anemia (hemoglobin 12.5 Gm.). Blood pressure was 130/80 mm. Hg. Serology was negative. She received only Seconal as medication, and the delivery was

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TABLE I. TWENTY-FIVE CASES WITH WENCKEBACH PERIODS AND ORGANIC CARDIOVASCULAR DISEASE

CASE	AGE (YR.)	SEX	DIAGNOSIS	DIGITALIS*	OTHER ECG FINDINGS	FOLLOW-UP
1.	42	M	RHD; failure	Leaf	Sinus tachycardia; atrial abnormality	Diagnosis confirmed by autopsy
2.	53	F	HCVD; failure	Digitoxin 0.2 mg./day	1° A-V block; myocardial abnormality	Expired 44th hospital day; no autopsy
3.	78	M	ASHD	None by history	Myocardial abnormality; later 1° A-V block	None
4.	49	F	Rheumatic carditis; failure	Leaf	Left ventricular strain	None
5.	69	M	ASHD; failure; old coronary occlusion	Leaf	Atrial flutter, left ventricular hypertrophy	Diagnosis confirmed by autopsy
6.	79	M	ASHD; failure	Leaf	Frequent atrial and ventricular premature contractions	Digitalis omitted; reverted to sinus tachycardia
7.	70	M	HCVD; failure	Leaf	Left bundle branch block	Pulse regular on subsequent visits
8.	75	M	HCVD; failure	Leaf	Left ventricular strain	Regular rhythm 7 mo. later
9.	77	F	ASHD; failure	Leaf	Nonspecific S-T and T changes	Regular rhythm 2 wk. later
10.	70	F	ASHD; failure	Leaf	Sinus bradycardia; nonspecific S-T and T changes	None
11.	35	F	HCVD; failure	None	Paroxysmal atrial tachycardia; atrial premature contractions	Digitalized 11 mo. later; became intoxicated on digitalis
12.	66	F	HCVD; failure; uremia	Digitoxin 0.1 mg./day	Left ventricular strain; VPC	Digitalis omitted 10 days; next ECG showed normal sinus rhythm
13.	76	M	HCVD; failure	Lanatoside C 1.4 mg.	Intraventricular conduction defect	On leaf maintenance rhythm changed to chronic atrial fibrillation

14.	70	M	HCVD; failure	None	Left ventricular strain	None
15.	45	F	RHD; mitral insufficiency; failure	Leaf	Bigeminy; nonspecific S-T and T changes	Digitalis omitted 3 days; ECG showed first degree A-V block
16.	78	F	HCVD; failure; atrial fibrillation	Leaf grains 1.28 alternated with grains 2.56	Frequent VPC; left ventricular strain	4 yr. later: atrial fibrillation with VPC
17.	70	F	ASHD; coronary insufficiency	Leaf	Left ventricular strain	Digitalis omitted; 3 wk. later ECG showed myocardial ischemia
18.	75	M	ASHD; acute posterior wall infarct	Leaf	Acute posterior wall infarct; VPC	1 day later, complete heart block
19.	66	M	HCVD; failure	None	Left ventricular strain	Digitalized 10 mo. later; had normal sinus rhythm
20.	70	M	HCVD	None	Left ventricular hypertrophy; atrial abnormality	8 mo. later, complete heart block; expired; no autopsy
21.	81	F	ASHD; failure	Leaf	Myocardial ischemia	None
22.	37	M	Sickle cell anemia; failure	Leaf	Nonspecific S-T and T changes; VPC	Expired 2 mo. later at home; no autopsy
23.	43	M	Paroxysmal atrial tachycardia, cause unknown	Lanatoside C IV 1.6 mg.	Paroxysmal atrial tachycardia	Digitalis discontinued; had sinus tachycardia 5 mo. later
24.	61	M	Chronic constrictive pericarditis	Gitalin 1.5 mg. daily for 5 days	Nonspecific S-T and T changes; low voltage	Wenckebach periods disappeared 5 days after digitalis discontinued
25.	36	F	Eclampsia	Lanatoside C IV 1.6 mg.	Left ventricular strain	Died 1 yr. later, again post partum, in shock; no autopsy

***That is, on digitalis at the time the Wenckebach phenomenon was detected. All medication was per os unless otherwise specified. At this institution digitalis leaf is used as routine maintenance therapy. The preparation used is Digitora (Upjohn). The tablets contain grains 1.28 leaf which equals 0.83 U.S.P. XV digitalis units which equals 83 mg. U.S.P. XV, reference standard which equals 1 U.S.P. X cat unit.**

RHD = Rheumatic heart disease. HCVD = Hypertensive cardiovascular disease. ASHD = Arteriosclerotic heart disease. VPC = Ventricular premature contractions.

accomplished without anesthesia. On delivery of the placenta the patient was given 0.2 mg. of methylergonovine intramuscularly and 0.2 mg. of the same drug intravenously.* At 3:00 P.M. a third dose of methylergonovine, 0.2 mg., was administered by mouth. At 7:00 P.M., four and one-half hours after delivery, the patient complained of palpitations, and an irregular heart rhythm was detected on physical examination. The electrocardiogram revealed the Wenckebach phenomenon. No other evidence of heart disease was discovered on clinical evaluation. The pulse irregularity disappeared spontaneously.

In July, 1956, the patient was admitted for the full-term, normal delivery of a live infant. Her pregnancy was uncomplicated; no irregularity of heart rhythm occurred with this delivery nor was there other clinical evidence of heart disease.

CASE 2.—G.M.D., a 23-year-old Negro woman (Gravida III, Para II), was admitted on Sept. 2, 1953, in labor. Past history revealed that the patient had been treated for syphilis in 1946; her serology was negative at the time of this pregnancy. On admission her blood pressure was 104/70 mm. Hg; pulse was 60 and irregular. The full-term delivery of a normal infant occurred at 6:09 P.M., on September 2, with intermittent Trilene inhalations as anesthesia. The patient received routine doses of methylergonovine. An electrocardiogram made on September 3, revealed sinus rhythm with a rate of 70 and first degree atrioventricular block.

On September 5, it was noted that the pulse was again irregular, and an electrocardiogram revealed sinus bradycardia with a rate of 58 and the Wenckebach phenomenon. Evaluation at this time revealed no evidence of heart disease.

The patient was seen in the Medical Clinic on March 18, 1954, complaining of "gas on stomach"; her pulse was found to be irregular and an electrocardiogram again demonstrated the Wenckebach phenomenon. She was treated with oral atropine sulphate, 0.2 mg., three times daily; and when she returned to the clinic on July 19, 1954, her heart rhythm was regular. No other clinical evidence of heart disease was found.

CASE 3.—M.E.R., an 18-year-old Negro woman (Gravida II, Para II), had the full-term delivery of a normal infant on Oct. 18, 1955. Serology was negative and the patient was normotensive. Saddle block anesthesia with Metycaine was used at delivery. Two oral doses of phenobarbital, 60 mg., and two intramuscular doses of sodium Amytal, 250 mg., were given ante partum. Pitocin (2.0 c.c. intramuscularly) was given at the time of placental delivery, followed by a 1.0 c.c. dose one hour post partum. The patient was discharged after an uneventful post-partum course. Post-partum checkup revealed a complaint of back pain; therefore, the patient was referred to the Medical Clinic on Dec. 6, 1955. Her pulse was found to be irregular, and an electrocardiogram revealed the Wenckebach phenomenon. The patient was promptly admitted for evaluation. Physical examination also revealed a Grade 2 systolic murmur at the cardiac apex. Hematocrit was 43 per cent; antistreptolysin 0 titer was 100 Todd units; C-reactive protein study was negative; cardiac fluoroscopy with barium swallow revealed no abnormality. An electrocardiogram made on December 16, revealed normal sinus rhythm. The patient had received no specific medication; she has not been examined since her discharge.

CASE 4.—L.B.S., a 25-year-old Negro woman (Gravida VII, Para VI), was seen on a routine ante-partum clinic visit on April 18, 1955. She was in the eighth month of pregnancy, and a pulse irregularity was discovered on physical examination. Serology was negative and the patient was taking no medicine. Blood pressure was 105/65 mm. Hg. An electrocardiogram revealed the Wenckebach phenomenon. The patient went to term and was delivered uneventfully on June 11, at which time her heart rhythm was regular. On Nov. 23, 1956, still another pregnancy was delivered at term with no evidence of heart disease.

CASE 5.—M.M., a 19-year-old Negro woman (Gravida II, Para I), with her last menstrual period on Oct. 19, 1953, was admitted on March 9, 1954, with the complaints of abdominal cramps and vaginal bleeding of three days' duration. Her pulse was noted to be irregular on admission, with a rate of 120, and a Grade 2 systolic murmur was audible over the precordium. Serology was negative and blood pressure was 100/70 mm. Hg. The fetus was delivered shortly after ad-

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***Routine post-partum medication at this hospital consists of methylergonovine, 0.2 mg., intravenously, and intramuscularly when the placenta is delivered, followed by methylergonovine, 0.2 mg., orally every four hours for a total of six doses.**

mission, and the patient received routine doses of methylergonovine. Vaginal bleeding continued, however, and on March 12, 1954, dilatation and curettage was performed under Metycaine saddle block anesthesia. Preoperatively the patient was given 10 mg. of morphine sulphate and 0.2 mg. of atropine sulphate. Postoperatively she received routine doses of methylergonovine. The pulse irregularity was noted again, and an electrocardiogram taken on March 14, revealed sinus bradycardia with the Wenckebach phenomenon. The patient was discharged still with her arrhythmia. This patient was seen again on March 4, 1957, in the eighth month of a later pregnancy in the Medical Clinic, where she had been sent for evaluation of a Grade 2 systolic murmur heard at the left sternal border. Her pulse was irregular at this time, and the electrocardiogram again revealed an intermittent Wenckebach phenomenon. Full-term delivery of a normal infant occurred on April 4, 1957, and the heart rhythm was regular. Studies done in the clinic prior to the last delivery failed to confirm a diagnosis of organic heart disease; the patient has not been seen since her last delivery.

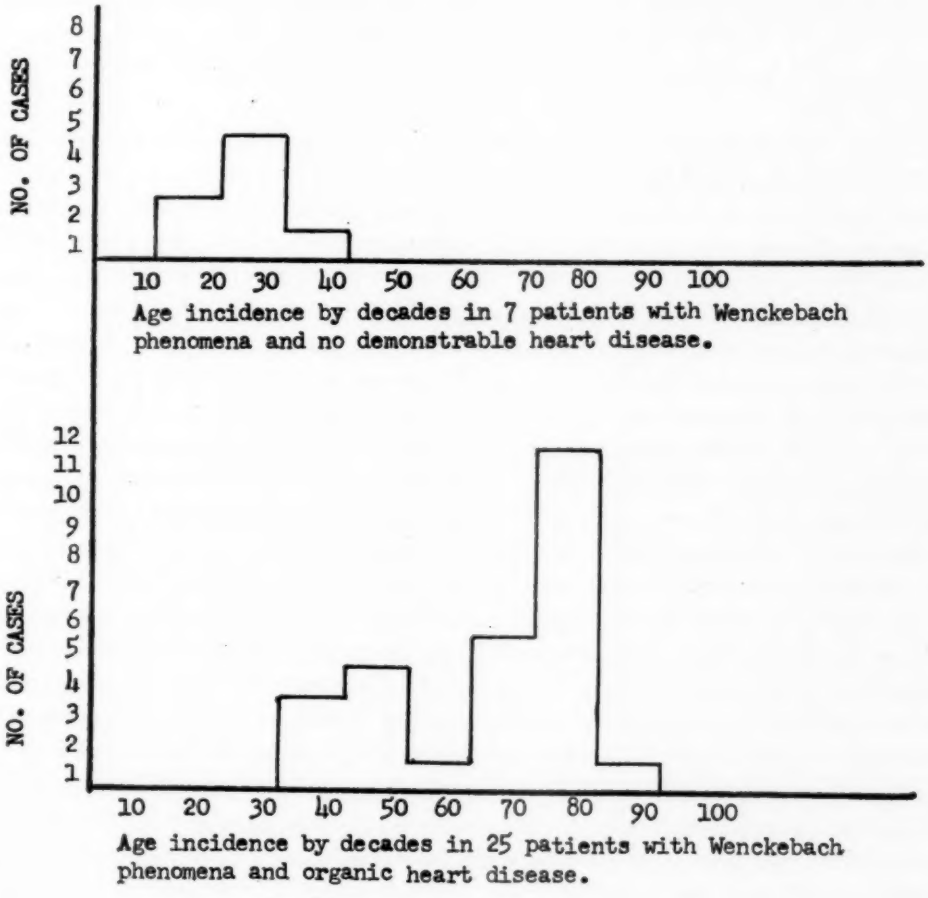

Fig. 1.

CASE 6.—E.H., a 26-year-old Negro woman (Gravida IV, Para III), was admitted on Feb. 7, 1957, at 12:40 A.M., in active labor. Serology was positive at one dilution but no evidence of cardiovascular syphilis was detected then or subsequently. A cardiac irregularity was noted on admission, and an electrocardiogram revealed right axis deviation and the Wenckebach phenomenon. The patient was normotensive. She was given 75 mg. of Demerol and 200 mg. of Seconal as preanesthetic medication. At 3:30 A.M. the patient was delivered of a normal infant

under nitrous oxide-oxygen anesthesia. Routine doses of methylergonovine were administered. An electrocardiogram taken at 4:15 A.M. revealed normal sinus rhythm. A chest film showed numerous calcific densities throughout both lung fields, but the cardiac silhouette was normal. It was thought that no chronic active pulmonary disease was present. This patient has not been seen since her discharge.

CASE 7.—(This patient was not pregnant.) M.K., a 33-year-old Negro woman (Gravida IV, Para IV), was admitted on July 16, 1955, for surgical treatment, with the diagnoses of chronic cervicitis, chronic pelvic inflammatory disease, and tubo-ovarian abscess. Her last menstrual period was June 28, 1955. Blood pressure was 118/60 mm. Hg; her pulse was irregular with a rate of 52. Serology was positive at two dilutions but no evidence of syphilitic cardiovascular disease was detected. No murmur was heard. An electrocardiogram demonstrated the Wenckebach phenomenon. Atropine sulphate, 0.2 mg., was administered subcutaneously and the arrhythmia disappeared. Hysterectomy and bilateral salpingo-oophorectomy were performed, and the patient was discharged on July 29, 1955. The Wenckebach phenomenon did not recur nor was there any complication during the postoperative period.

DISCUSSION

Since Wenckebach[1,2] first described the variation of second degree atrioventricular block which bears his name, Wenckebach periods have been described in a number of clinical situations, for the most part associated with organic heart disease or drug intoxication. Recently, Wenckebach periods have been reported with anxiety alone,[3] in young men otherwise completely healthy,[4] and experimentally by repeated vagal stimulation of the nonperfused frog's heart.[5] In an analysis of the electrocardiograms in 1,000 healthy young aviators no Wenckebach periods were reported by Graybiel and associates[6,7]; however, 11 instances of prolonged P-R intervals were found in the absence of clinical evidence of heart disease, and 6 of these persisted for 10 years. Review by Manning[8] of the electrocardiograms of 5,000 Canadian applicants for aircrew training revealed no Wenckebach periods, but again 23 subjects showed prolonged P-R intervals in the absence of clinical heart disease. In 14 of these, repeat electrocardiograms showed either a normal P-R interval or one that could be brought within normal limits either by assuming the upright posture or by respiratory maneuvers. The normal electrocardiogram in pregnancy has been well documented by Zatuchni,[9] Bettencourt and associates,[10] and Fragoso.[11] Complete heart block in pregnancy has been reported a number of times, and the literature on the subject has been reviewed.[12,13] An organic etiology was described for most of these cases.

Sir Thomas Lewis[14] stated that heart block resulted clinically from the same causes that produce it experimentally, namely, (1) lesions of the conducting tract, (2) vagal stimulation, and (3) poisoning (digitalis intoxication being the classical example). Modern texts restate this general concept.[15] A probable mechanism in Wenckebach periods has been presented by Decherd and Ruskin.[16] These authors state that the following factors determine the sequence of atrioventricular conduction in the Wenckebach type of block: (1) duration of complete refractoriness, (2) duration of partial refractoriness, (3) contour of the recovery curve (a curve obtained by plotting P-R against the preceding R-P interval), (4) conduction time after complete recovery, and (5) atrial rate. The five factors listed above are said to be mutually interdependent and may change simultaneously in the same or opposite directions. Thus, acceleration of atrial rate which

would tend to increase atrioventricular block, in itself shortens refractoriness and recovery, in effect shifting the recovery curve upward and to the left. Increased vagal tone shifts the recovery curve in the direction of less rapid recovery and greater block but may be associated with a slower atrial rate which would allow more complete recovery. In essence, the Wenckebach type of partial atrioventricular block is explained on the basis of varying atrial rates and varying curves of recovery of atrioventricular conductivity.

In our cases no organic heart lesions could be demonstrated by clinical means. The only drug these patients received in common was methylergonovine (4 of 7). It is stated authoritatively that ergonovine lacks sympatholytic action.[17] Other drugs received by these individuals also lacked this action. Current physiology texts cite no accentuation of parasympathetic function in pregnancy or labor.[18,19] This leaves intrinsic humoral mechanisms to be considered.

In a recent paper, Lown and co-workers[20] suggested that the C 11-oxysteroids participate in the regulation of atrioventricular conduction. Following up the work of Somerville and associates,[21] Lown confirmed the tendency toward P-R prolongation in adrenal insufficiency and demonstrated the converse to be true in Cushing's syndrome. It has further been reported that 54 of 66 patients with heart block due to rheumatic carditis responded to steroid therapy with return of A-V conduction to normal.[22] Cortisone therapy has been reported to shorten the P-R interval even when no inflammatory lesion exists in the myocardium.[23]

The possibility was considered that perhaps the known hormonal changes in pregnancy might participate in producing the changes in A-V conduction here observed. It has been reported that 17 hydroxycorticosteroids as a group start increasing early in pregnancy, reach a level about seven times the normal nonpregnant level immediately after delivery, and then drop off, returning to the nonpregnant level by the sixth post-partum day.[24] It would be expected from what is now known that this should enhance rather than impede A-V conduction.

Chorionic gonadotrophin reaches its peak elevation about the seventh week of pregnancy, falls to a relatively low level, then rises slightly again near the time of delivery.[25] Circulating estrogenic activity reaches a peak around the thirty-eighth week and then drops off slightly before delivery.[25] Circulating progesterone, on the other hand, is reported to be normal or low during the last two trimesters of pregnancy but rises at the time of delivery.[26] Significant amounts of ACTH have also been found in placental tissue.[27] We know of no reports linking these changes with A-V conduction at all; it is quite possible that the occurrence of the Wenckebach periods in our 6 pregnant patients is no more significant than their occurrence in the one nonpregnant patient. It remains of interest to speculate on the influence, if any, that these humoral fluctuations might have on A-V conduction. Finally, it should be noted that while 6 out of 7 patients found to have Wenckebach periods were pregnant or post-partum women, the over-all incidence was roughly 1 per 10,000 live births at this hospital.

SUMMARY AND CONCLUSIONS

Twenty-six thousand and ninety-three electrocardiograms have been reviewed. Thirty-two instances of Wenckebach periods were found. Of these,

25 had organic heart disease and/or were on digitalis medication. Seven patients had no demonstrable heart disease; of these, 6 were pregnant. The possible significance of this rare finding as related to the humoral changes of pregnancy is discussed.

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Simultaneous Atrial Flutter and Ventricular Tachycardia

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The association of ventricular tachycardia and atrial flutter is extremely rare. It was demonstrated once by Gallavardin[5] and mentioned by McMillan and Bellet.[2] The following case history presents a recording of the simultaneous presence of ventricular tachycardia and auricular flutter.

CASE REPORT

On March 25, 1956, a 74-year-old woman was admitted to the Neoplastic Service at Montefiore Hospital for the treatment of an ulcerating carcinoma of the right breast and ipsilateral arm edema and pain due to axillary metastases. A known diabetic for 9 years, she was without glycosuria on a controlled diet. No history of cardiovascular or renal disease could be elicited. The blood pressure on admission was 160/90 mm. Hg; her heart rate was 80 per minute with regular rhythm. No murmurs were heard. A roentgenogram of the chest revealed left ventricular enlargement but no pulmonary or mediastinal metastases. The admission electrocardiogram was normal. The rhythm was of sinus origin and regular. The duration of the QRS complex was 0.08 second (Fig. 1). Cobalt radiation was administered in an attempt to slow the progression of her disease. Thoracic, subarachnoid, and stellate ganglionic blocks did not relieve her pain.

On Aug. 20, 1956, in her fifth month of hospitalization, an episode of anterior chest pain occurred. The electrocardiogram of that day did not differ from the one on admission. Mild hypotension necessitated the use of Wyamine for 24 hours. There were no signs of congestive heart failure. On August 21, the electrocardiogram revealed RS-T elevation in Leads I and aV_L and depression in Leads V_1 to V_3 (Fig. 2,*A*). The serum glutamic oxalacetic transaminase 18 hours after the onset of chest pain was 85 units per milliliter per minute (normal 5-40). Further RS-T elevation in Leads I and II were noted in the tracing of August 24 (Fig. 2,*B*). Her complaints subsided gradually, only to have dyspnea occur on August 27, 7 days after the episode of chest pain. That afternoon the patient went into pulmonary edema. Cedilanid, 1.2 mg., was given intramuscularly. An electrocardiogram 2 hours after administration of the digitalis preparation showed aberrant ventricular complexes of 0.12 second duration. These complexes were regular, occurring at a rate of 157 per minute. No definite atrial activity was discernible (Fig. 3). An esophageal lead was passed. At atrial levels there were sharp biphasic complexes at a rate of 273 per minute with an undulating base line (Fig. 4,*A* and *B*). Ventricular complexes were slower than, and unrelated to, atrial activity; the ventricular rate was identical to that seen in the standard leads (Fig. 4,*A*, *B*, and *C*). Eighteen hours after the patient had received the single dose of Cedilanid, and while she was without additional medication, and without hypotension, her electrocardiogram demonstrated a regular sinus rhythm, with multiple premature ventricular contractions coming singly or in runs of 2 to 5. The rate of the runs of ventricular

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premature beats and the configuration of these complexes were identical to the ventricular complexes seen during the combined ventricular tachycardia and atrial flutter (Fig. 4,*C*, *D*, and *E*). Over the next 10 hours 1.8 Gm. of quinidine was given in divided doses, and a maintenance regimen of 1.6 Gm. of oral quinidine sulfate per day was started. The tracing of August 30, and subsequent ones, showed regular sinus rhythm with multiple atrial extrasystoles. RS-T depression and Q-T prolongation in the precordial leads suggested quinidine effects (Fig. 5). The patient remained without signs or symptoms of heart failure. She was discharged after 7 months of hospitalization, without cardiac medication.

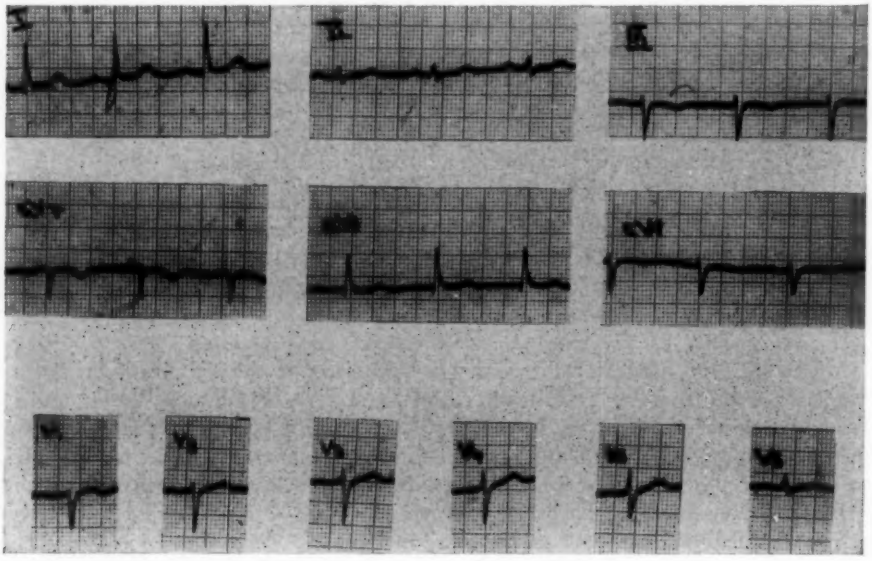


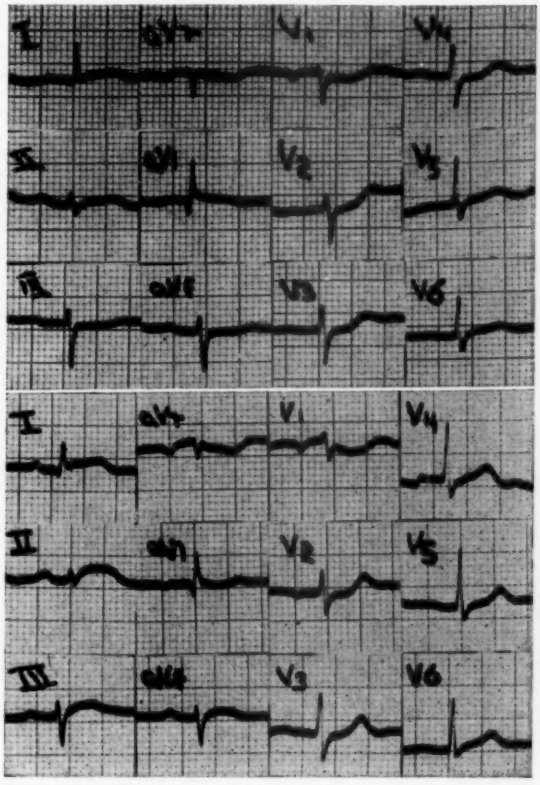
Fig. 1.—Admission electrocardiogram: regular sinus rhythm with normal ventricular conduction.

DISCUSSION

Gallavardin[5] described the simultaneous, repetitive occurrence of two arrhythmias in an elderly male with syphilitic aortitis who was receiving digitalis for treatment of atrial flutter. Tracings before and after a paroxysm of ventricular tachycardia indicated normal ventricular conduction and ventricular premature contractions of a configuration similar to those of the paroxysm. During the paroxysm of ventricular tachycardia, atrial activity could not be discerned, but the ventricular rate was in no way a fraction of the previous atrial activity. This report would appear to have presented an example of simultaneous atrial flutter and ventricular tachycardia, although simultaneous demonstration of the two rhythms was not accomplished. McMillan and Bellet[2] described two cases of ventricular tachycardia in the presence of atrial flutter. No tracings were presented. No other examples were found in our review of the literature.

When the tachycardia was first studied in the present case, the routine electrocardiogram failed to reveal the true nature of the arrhythmia. Since atrial activity was not clearly demonstrated, the differentiation of supraventricular tachycardia with bundle branch block from ventricular tachycardia could not be made. The demonstration of ventricular tachycardia in the esophageal lead

A.



B.

Fig. 2.—*A*, Electrocardiogram taken at the onset of chest pain, August 21. There is regular sinus rhythm, RS-T elevation in Leads I and aV_L, and RS-T depression in Leads V_{1-3}. *B*, Electrocardiogram taken 3 days later, August 24, showing persistent elevation of the RS-T segment in Lead I, and also elevation of RS-T in Lead II.

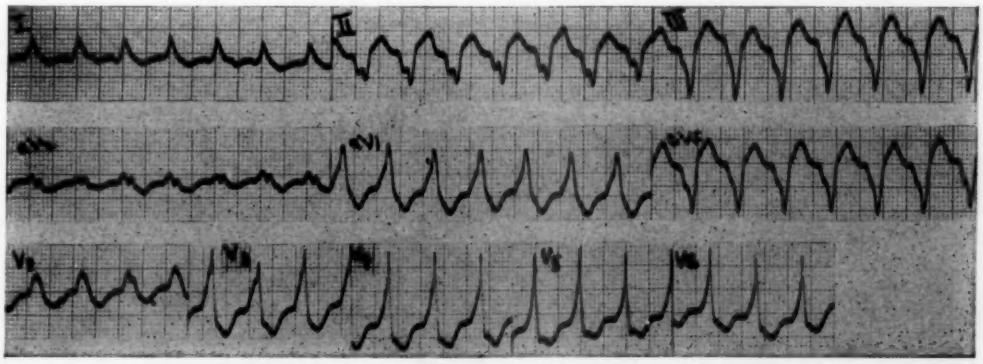


Fig. 3.—Electrocardiogram taken on August 27, at the onset of pulmonary edema. There is regular ventricular activity at a rate of 157 per minute. The QRS complexes are of 0.12 second duration. Atrial activity is not definitely discernible.

is indisputable. Ventricular activity was completely dissociated from atrial activity. The ventricular complexes were aberrant in form, and 0.12 second in duration. Furthermore, on the following day, when the basic rhythm was of sinus origin, the ventricular extrasystoles were identical in form to those seen

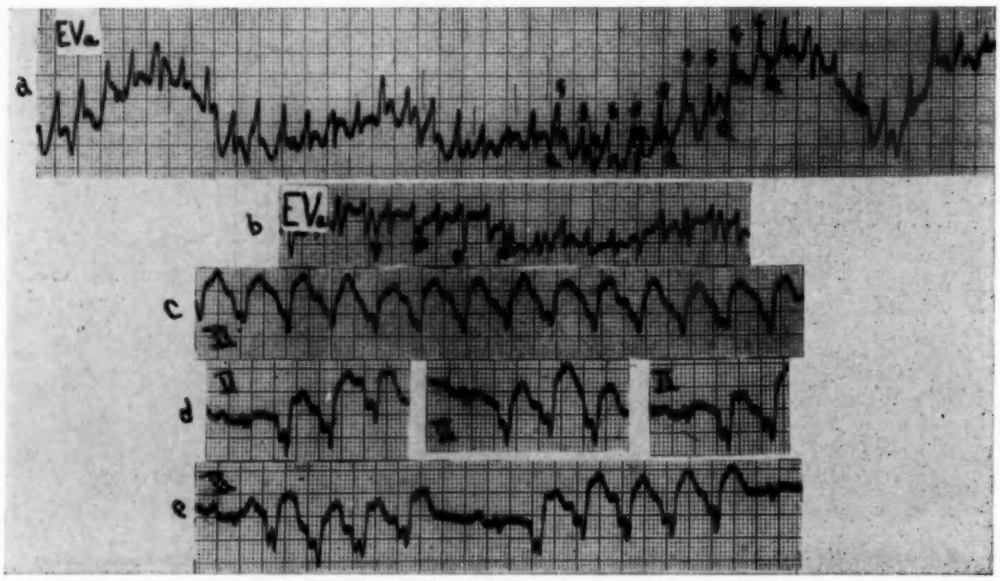


Fig. 4.—*A* and *B*, The esophageal electrocardiogram of August 27, shows regular atrial activity, with sharp biphasic complexes occurring at a rate of 273 per minute on an undulating base line. The QS of ventricular activity may be seen between the F waves, or distorting the latter. These QS complexes occur at a rate identical to that of complexes seen in the Lead II that was taken at the same time (*C*). *D* and *E*, The electrocardiograms of August 28. The rhythm is regular sinus with runs of ventricular extrasystoles. The configuration and rate of the extrasystolic complexes are identical to those of the ventricular complexes during the double tachycardia of the day before (*C*). The ventricular complexes of *A*, *B*, *C*, and *D* are matched; complexes in *A* and *B* may be found directly over those in *C* or *D*.

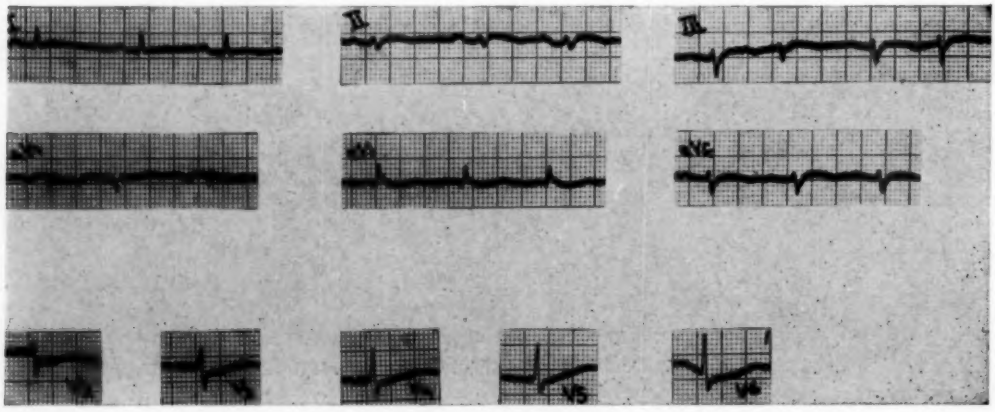


Fig. 5.—The electrocardiogram of August 30. There is a regular sinus rhythm with occasional atrial premature beats. RS-T segment depression and QT prolongation are present in the precordial leads.

during the tachycardia. In addition, the sphygmic interval of the runs of extrasystoles and that of the tachycardia were the same. The simultaneous presence of atrial flutter was not suspected. It was not seen in the routine leads (Fig. 3) but was discernible in the esophageal tracing (Fig. 4, *A* and *B*). The atrial rate was too rapid to have been atrial tachycardia, and the interval between the biphasic complexes was not isoelectric but undulated as in atrial flutter.[4,6]

Gallavardin considered this double rhythm simply a terminal event. Postmortem examination in his patient failed to reveal gross evidence of encroachment of the primary syphilitic process upon the coronary ostia, nor was myocardial fibrosis grossly evident. McMillan and Bellet[2] attributed the arrhythmias to digitalis.

The presence of chest pain, RS-T segment deviation, and elevated transaminase suggests recent myocardial infarction as the cause of the double tachycardia in this case.[3,7,8] However, since the electrocardiogram was not obtained immediately prior to the administration of digitalis, digitalis toxicity cannot be ruled out as a cause of the arrhythmia.[1,2]

SUMMARY

A case of simultaneous ventricular tachycardia and atrial flutter is presented. The esophageal electrocardiogram clearly demonstrated the nature of the double rhythm which was not diagnosed from the routine 12-lead electrocardiogram. The etiology of the arrhythmias was most likely a recent myocardial infarction, although digitalis toxicity could not be excluded.

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Congenital Mitral Atresia

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Congenital mitral atresia as a cardiac anomaly is incompatible with life for a long period. Only temporarily is a postnatal circulation possible if the hypoplastic left ventricle, which occurs in a close causal connection with mitral atresia, is sufficiently bypassed. The etiology of this malformation of the heart is still unknown. Besides maternal infections, such as rubella or syphilis, heredity, alcoholism, and early developmental disturbances during the second month of intrauterine life must be accounted for as pathogenic factors. Several theories are based on aberrations in the usual bending of the primary cardiac tube (Spitzer's theory, quoted by Doerr[16]), fusion between the septum primum and the endocardial cushions (Brockman[56]), maldirected growth of the interatrial and interventricular septum (Moenckeberg[44]), or uneven partitioning of the truncus arteriosus (Castrovinci and Cucci[52]).

Disregarding the gross cardiac anomalies, which involve the whole cardiovascular system by "complete transposition" (Abbott[53]) of the great vessels, and which are sometimes also associated with mitral atresia[54,57,58] but belong to a variety of malformations without any uniform physiopathologic picture, congenital mitral atresia occurs in two different forms: (1) isolated, without marked diminution of the arterial outlet, and (2) combined with atresia or high-grade hypoplasia of the ascending aorta.

The extreme Lutembacher's syndrome, as isolated mitral atresia may also be called (Rossi[12]), is a pathologic rarity. In the literature we discovered 16 reported cases.[1-14,44] They are somewhat divergent as clinical and pathologic entities but conform insofar as they all revealed an isolated mitral atresia. Table I gives the main data on these 16 cases and includes data on Case 1 presented in this communication.

During lifetime, isolated congenital mitral atresia can hardly be diagnosed.[57] Its clinical appearance varies from case to case, and although Taussig[15] has stated that certain changes in the contours of the x-ray picture of the heart suggest a single ventricle or, more generally, a cardiac malformation, the exact classification is only possible on autopsy.

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TABLE I. SEVENTEEN CASES OF ISOLATED MITRAL ATRESIA

AUTHOR	AGE	SEX	FORAMEN OVALE	INTERVENTRICULAR SEPTUM	DUCTUS ARTERIOSUS	AORTA
Borow and Dimaio[6] (Case 1)	2 days	F	closed	defect	closed	dextroposed, hypoplastic
Donnally[1]	2 days	F	patent	intact	patent	rudimentary (mitral valve: extreme stenosis)
Edwards and DuShane[2]	27 days	F	closed	small defects	patent	normal size
Edwards and Rodgers[3]	4 mo.	M	patent	defect	closed	normal size
Friedman, Murphy and Ash[11] (Case 1)	10 days	F	patent	defect	patent	dextroposed
Friedman, Murphy and Ash[11] (Case 2)	4 mo.	M	patent	defect	patent	dextroposed
Jost[7]	7 days	F	patent	several defects	widely patent	coarctation
Large[4] (Case 1)	14 days	M	patent	defect	patent	dextroposed
Lawrence and Nabarro[5]	3½ mo.	F	patent	defect	patent	overriding
Moenckeberg[14]	—	—	patent	intact	—	narrowed aorta ascendens
Rossi[12]	1 day	M	closed	gross defect	closed	—
Scriba[8]	stillborn	F	patent	defect	patent	overriding
Smulders and Voussure[14]	11 days	M	patent	defect	patent	dextroposed
Spolverini and Barbieri[9] (Case 7)	40 days	M	slit-shaped	defect	closed	overriding
Theremin[10] (Case 106)	2 days	M	closed	defect	patent	overriding
Voussure, Zylberszac and Pelc[13]	50 days	M	patent	gross defect	patent	normal size
Teller (Case 1)	16 days	F	patent	gross defect	patent	slightly narrowed

The other group of congenital mitral atresia, wherein this condition is associated with atresia or marked stenosis of the aorta, appears more frequently. Seventy-two cases were collected from the literature.[7,10-12,15,17-52,54] Many of them had other congenital anomalies in addition to the mitral and aortic atresia (See Refs. 7, 14, 21, 28, 38, 48, 52, 56, and Case 2 presented in this paper). Consequently connected with an atresia of the mitral valve is a hypoplasia of the left heart, especially of the left ventricle. In most of the reported cases the left ventricle did not seem to have functioned at all. The hemodynamics are thus fundamentally changed, and will be discussed more thoroughly later.

The life expectancy of infants born with atresia of the mitral valve is very poor: more than 70 per cent of the reported cases had died within the first postnatal days. The longest survival was 19 weeks, as reported by Nadas.[54] Edwards and Rodgers,[3] Rossi,[12] and Friedman, Murphy and Ash[11] each mentioned a patient who lived 4 months. Death usually ensued under the signs of congestive heart failure. No promising specific treatment of atresia of the mitral valve is yet known, and the diagnostic procedures, such as cardiac catheterization or angiography, are greatly limited on account of the babies' severe general condition.

Following is a report on the histories, clinical courses, and autopsy records of 2 patients with congenital mitral atresia encountered during the past 2 years. One case revealed an isolated atresia of the mitral valve with only slight narrowing of the ascending aorta, while the other presented a combined aortic and mitral atresia.

CASE REPORTS

CASE 1.—J.D., a 16-day-old white female infant, was born at full term to a healthy 26-year-old mother, para II, gravida III. The course of the gestation had been uneventful. There was no history of infection. The delivery was spontaneous under ether anesthesia. Duration of labor was 6 hours and 30 minutes. The blood Wassermann was negative.

Clinical History.—At birth the baby appeared normal and weighed 5 pounds and 10½ ounces. No cyanosis was observed and no cardiac murmur heard. The blood count disclosed the following: 5,150,000 RBC; 103.2 per cent hemoglobin; 13,800 WBC. The urinalysis was normal. A few hours after birth the infant developed slight cyanosis on movement; this condition was accentuated with crying. In the next few hours the cyanosis became more pronounced, even with the infant exposed to continuous oxygen. A physical re-examination revealed diminished breath sounds but maximal heart sounds over the right side of the chest. No murmur was apparent.

Chest X-Ray.—Examination of the chest revealed the entire right lung field to be greatly obscured by a homogeneous density which may have represented either a congenital absence of the right lung or a widespread atelectasis of this lung. There was no definite cardiac silhouette which could be identified. The left lung appeared well aerated and clear. The left leaf of the diaphragm was not unusual and the costophrenic angle was clear.

Further Clinical Course.—The diagnosis of almost complete atelectasis of the right lung associated with actual or symptomatic dextrocardia was very suggestive; therefore, treatment with oxygen inhalation, resuscitation upon cyanosis, and careful feedings (by gastric gavage) was continued. The respirations became progressively rapid and shallow, and the cyanosis increased. The general condition of the child deteriorated steadily, and on the sixteenth day of life it died in an attack of impaired respiration.

Post-Mortem Examination.—The subject was a 16-day-old white female infant, measuring 48 cm. in height and weighing approximately 3,000 grams. The body was rather cyanotic, especially at the head and upper extremities. The fingernails did not reach the level of the finger-

tips. The minor labias were not covered by the major ones. The clitoris appeared somewhat hypertrophied. Both the gluteal areas revealed numerous marks from injections. Livor mortis was present as well as rigor mortis.

Opening of the thorax showed the right chest cavity to be almost completely occupied by the enlarged heart. The pericardial sac was adherent to the lateral chest wall. The left chest cavity contained the enlarged left lung which did not collapse. The pericardial sac was carefully peeled off the chest wall, revealing the hypoplastic right lung, which was situated in the posterior costophrenic angle. The contents of the pericardial sac were a small amount of clear amber fluid.

The heart consisted mainly of the hypertrophied and dilated ventricular part and the hugely dilated right auricle. The incision into the right ventricle revealed a wide interventricular septal defect (2 x 2 cm.) which caused gross communication between the right and the left heart. The tricuspid opening was dilated and the valve apparently incompetent. The pulmonary artery was wider than normal at its cone and supplied mainly the left lung. A widely patent ductus arteriosus connected the pulmonary artery to the aorta, which was situated on the left side. The right branch of the pulmonary artery was quite narrow and hypoplastic. The ascending aorta arose from the left ventricle at the proper place but was somewhat narrowed. Its main branches, including the innominate artery, left subclavian, and left common carotid artery, were normally developed and situated. Distal to the mouth of the ductus arteriosus the aorta acquired its normal width and size. The pulmonary veins emptied on the left side of the heart into a small hollow which represented the hypoplastic left auricle. The mitral valve was atretic. The communication with the systemic circuit was sustained by a widely open foramen ovale (5 x 7 mm.). The pulmonary veins coming from the hypoplastic right lung were very small and thin.

The left lung was ordinarily developed and appeared hyperexpanded. The pulmonary parenchyma was edematous without areas of increased consistency or consolidation. The right lung contained a small amount of air in its peripheral portions, which was revealed by the positive floating test. The subdivision into three lobes could not be detected. The trachea and main bronchi were ordinarily developed.

Opening of the abdomen revealed the peritoneum to be smooth and shiny. The liver was enlarged, showing a dark blush-red discoloration. The pattern of the parenchyma was changed insofar as the centers of the lobuli were dark while the periphery appeared somewhat lighter yellow. These findings were most pronounced at the inferior posterior portions of the right lobe.

The spleen had a normal shape and size and ordinary consistency. It was surrounded by two larger and longer shaped and two smaller and round shaped accessory spleens. The stomach was considerably distended. The remaining gastrointestinal tract was patent without portions of atresia. The cecum had rotated as far as the location of the hepatic flexure. Its mesentery was rather flaccid. The kidneys were not unusual in appearance. They had pronounced renculi marcation. The ureters were patent and emptied into the urinary bladder which was filled with a small amount of clear urine. The uterus was divided into two horns. The ovaries could not be detected and seemed to be aplastic.

The *anatomic diagnosis* was congenital malformation of the heart (interventricular septal defect, hypoplasia of the left atrium with atresia of the mitral valve, slight hypoplasia of the ascending aorta, patent ductus arteriosus, and widely patent foramen ovale), hypoplasia of the right lung with underdeveloped vascular supply, emphysema and edema of the left lung, congestion of the liver, four accessory spleens, incomplete rotation of the cecum, uterus bicornis, aplasia of the ovaries.

CASE 2.—H.M., a 15-day-old white female infant, was delivered spontaneously from a 38-year-old mother at full term. The mother was para VI, gravida VII. The previous pregnancies had been uneventful, but during the whole time of this gestation she did not feel too well. However, her blood pressure was normal and the repeated urinalysis did not disclose pathologic findings. There was no history of infection. The blood Wassermann was negative. Labor was induced by instrumental rupture of the membranes and four injections of Pitocin. The duration of labor was 2 hours and 40 minutes. The delivery was spontaneous under inhalations of Trilene.

Clinical History.—At birth the infant appeared healthy. It weighed 7 pounds and 9 ounces and was 54 cm. long. There was no cyanosis. Physical examination revealed a blowing systolic murmur with accentuation of the second sound. The heart beats were somewhat rapid. Liver

and spleen were not enlarged. The blood count disclosed the following: 5,040,000 RBC; 16,500 WBC; 102 per cent hemoglobin. The rh-factor was negative. The Coombs test was negative. The urinalysis revealed a slight trace of albumin.

Chest X-Ray.—Examination of the chest revealed the leaves of the diaphragm and the costophrenic angles to be clear. The heart was minimally enlarged in its transverse diameter, chiefly toward the left. The upper mediastinum was not unusual. The vascular markings were prominent in both hilar areas, and there was one small patchy area of increased density in the right hilus, which may have represented a small area of pneumonitis. The peripheral portion of both lung fields showed minimal emphysematous changes bilaterally.

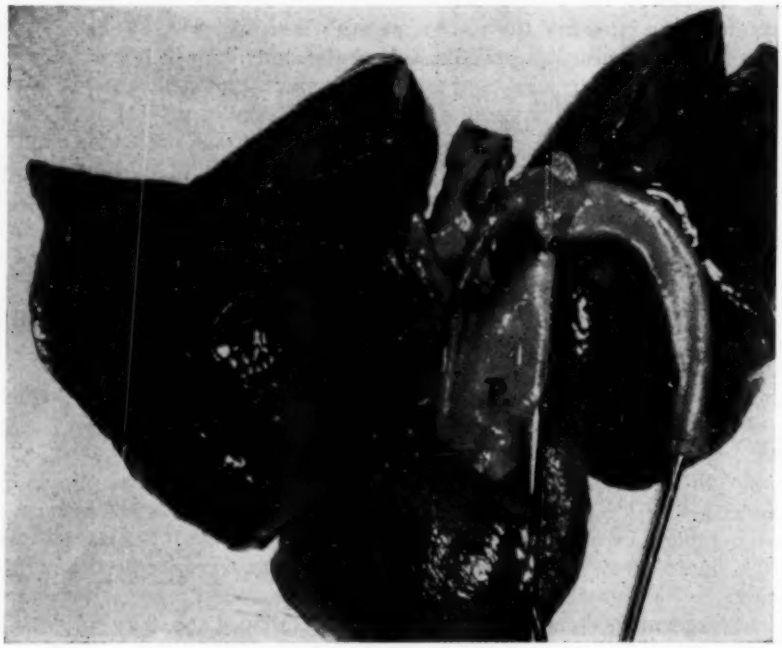

Fig. 1.—Case 2. Anterior view of the heart-lung specimen. *T.* = trachea; *i.A.* = innominate artery; *A* = aorta; *D.a.* = ductus arteriosus; *P.* = pulmonary artery.

Further Clinical Course.—According to the physical and roentgenographic findings the diagnosis of congenital malformation of the heart with possible septal defect could be established. Two days after birth the infant began to turn cyanotic upon crying. It was therefore temporarily placed in oxygen, which improved the cyanosis. The heart murmur remained unchanged. The feedings were taken fairly well without vomiting. The temperature was slightly elevated. During the following week attacks of cyanosis recurred more frequently. They were associated with tachycardia and labored respirations. The infant's general condition deteriorated steadily. Death ensued on the fifteenth day after birth.

Post-Mortem Examination.—The subject was a 15-day-old white female infant, measuring 54 cm. in height and weighing 3,600 grams. The signs of maturity were present. The development seemed to be ordinary. Marked cyanosis of the head and lateral portions of the trunk was present. There also were mottled cyanotic areas scattered over the chest and abdomen. Rigor mortis was present. No external injuries could be detected.

Opening of the thorax revealed that both lungs were ordinarily developed and expanded, but somewhat consistent. From the cut surface, frothy, sanguineous fluid could be expressed.

The thymus had the required size in regard to the age of the subject. A few subcapsular ecchymoses of pinhead size were disclosed.

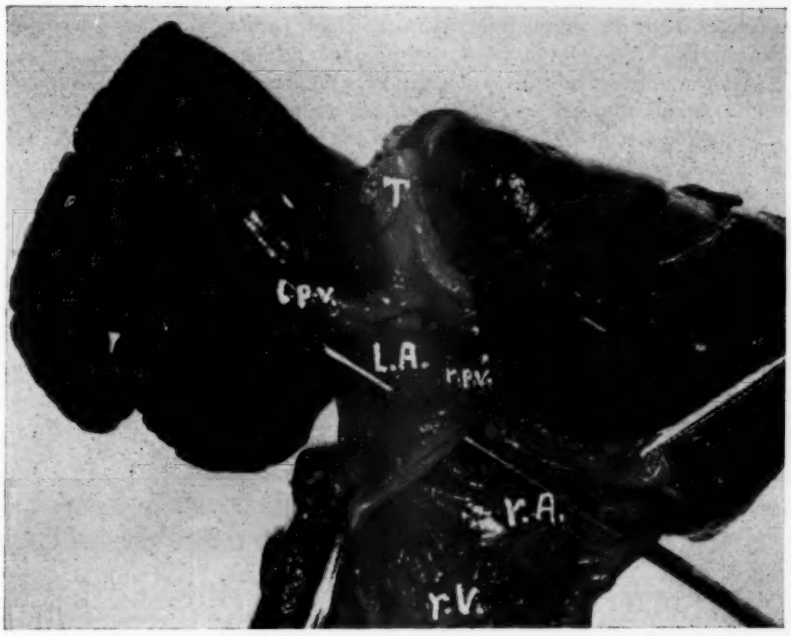

Fig. 2.—Case 2. Posterior view of the heart-lung specimen. *T* = trachea; *l.p.v.* = left pulmonary vein; *r.p.v.* = right pulmonary vein; *l.A.* = left atrium; *r.A.* = right atrium; *r.V.* = right ventricle. The probe is passed through the foramen ovale.

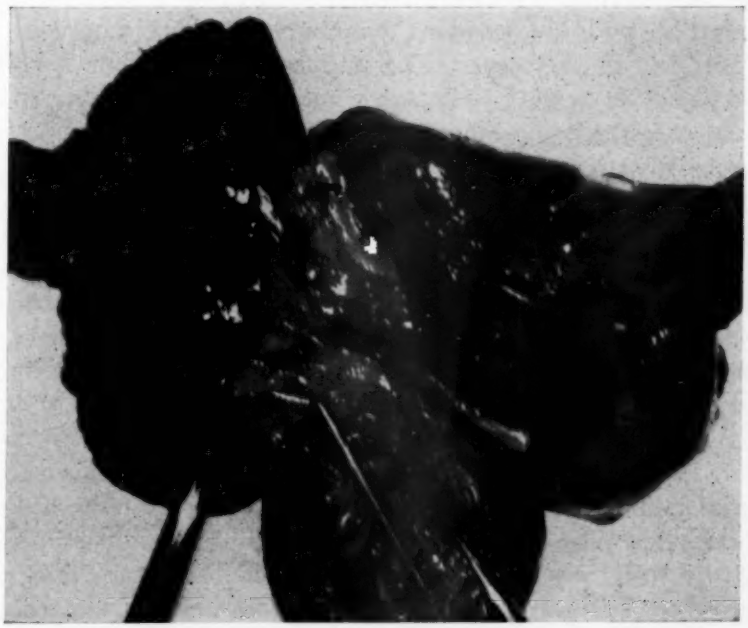

Fig. 3.—Case 2. Posterolateral view of the heart-lung specimen. *T* = trachea; *lV* = left ventricle; ● = site of the atretic mitral orifice; * = ridge of the interventricular septum. The probe is passed through the interventricular septal defect.

The pericardial sac contained a small amount of clear amber fluid. The heart was grossly enlarged, especially in its upper posterior portion which belonged to the auricular part. The vascular outlet consisted of one large trunk, the pulmonary artery, arising from the right ventricle and dividing into three branches. Two of them supplied the lungs. The middle one continued as ductus arteriosus and emptied into the aorta, maintaining the width and size of the original pulmonary trunk. The aortic arch and the descending aorta were situated on the left side. The ascending aorta was very narrow and hypoplastic up to the offspring of the innominate branch, where it acquired its normal size. The aortic orifice to the right of the pulmonary trunk was atretic. The pulmonary veins entered a small hollow on the left side of the heart, which represented the rudimentary left atrium. It communicated with the hugely dilated right atrium by a widely patent foramen ovale. The mitral opening was atretic, and no connection between the left auricle and the left ventricle could be disclosed. The latter was a minute cavity, merely appending on the dilated right ventricle, and separated from it by a small ridge of the incomplete interventricular septum. The septal defect measured 1.0 cm. in diameter. The musculature of the enormous right ventricle was hypertrophied and averaged 0.7 cm. in thickness. The right atrioventricular ostium was markedly dilated. The leaflets of the tricuspid valve were functionally incompetent and revealed pink, warty granulations at their margins. The branches of the aorta were normally developed and took origin in the usual manner.

The liver appeared to be slightly enlarged but was of normal consistency and color. The spleen was enlarged and of increased consistency. The remaining abdominal organs were not remarkable.

The *anatomic diagnosis* was congenital malformation of the heart (hypoplasia of the left ventricle and auricle, atresia of the mitral and the aortic valves, interventricular septal defect, patent foramen ovale, hypoplasia of the ascending aorta, and widely patent ductus arteriosus—see Figs. 1-3), fresh endocarditic changes at the tricuspid valve, pulmonary edema, congestion of liver and spleen.

COMMENT

During the fetal stage, mitral atresia combined with hypoplasia of the left heart is compatible with life because the main circulation circumvents the underdeveloped portions of the heart. The pulmonary blood flow is minimal and, therefore, no strain lies upon the left auricle and ventricle. This condition changes at birth: now the expanding lungs require an increasing blood supply, which in return progressively enhances the burden on the left heart. Because of the atresia of the mitral valve the stream of oxygenated blood has to pass the widely patent foramen ovale in a left-to-right shunt in order to join the systemic circulation. In cases with an additional aortic atresia the other supposition for postnatal circulatory function is the maintenance of a pathway from the right heart to the aorta by means of a patent ductus arteriosus.

In both our reported cases the mitral atresia was associated with a rudimentary left ventricle. The latter consisted of a small cavity merely appending to the functioning right ventricle. It was filled with blood via the interventricular septal defect. Despite the fact that the systemic circuit was furnished only with mixed arterial and venous blood, cyanosis occurred gradually and was absent shortly after birth. We agree with Friedman, Murphy and Ash[55] that the onset of cyanosis and respiratory distress after a period of absence of symptoms can be attributed to an insufficient arterial-venous reflux (left-to-right shunt) through the foramen ovale. This inadequate arterial return may increase slowly along with the steadily growing pulmonary circulation and subsequent filling of the left auricle. As was true in most of the reported cases, the infants of the

present report also finally succumbed to congestive heart failure and severe anoxemia. Their survival of 16 and 15 days, respectively, lies within the upper ranges of what could be expected according to the communications in the literature.

Case 1 revealed an obstruction of the mitral valve and a normally formed, slightly narrowed ascending aorta. The cardiac malformation was combined with other congenital anomalies of various organs (such as reported in the cases of Donnally[1] and Lawrence and Nabarro[5]). Whether or not the hypoplasia of the right lung was secondary to or independent of the developmental error of the heart remained undetermined.

On account of the systolic murmur and the enlarged contours of the heart on the x-ray pictures, Case 2 was recognized early as being a case of congenital cardiac malformation. A more detailed classification, however, was not possible before autopsy, when an atresia of the aortic and the mitral valves was disclosed. Functionally, this heart could be considered a "cor biatriatum triloculare." It resembled those reported by several other authors.[4,11,12,17,18,27,29,43,49,50] The endocarditic changes at the tricuspid valve most likey developed during the short period of extrauterine life. We do not assume an intrauterine infection since the pregnancy record of the mother was noncontributory.

SUMMARY

After a review of the literature concerning congenital mitral atresia, two more cases with this cardiac malformation are presented. This condition occurred in newborn white females who died 16 and 15 days, respectively, after birth. In both instances the mitral valves were atretic, the left auricles and the left ventricles hypoplastic. The second case also revealed atresia of the aortic valve and endocarditic changes of the tricuspid valve. Both hearts could temporarily maintain the circulation because of a functioning foramen ovale and a patent ductus arteriosus. The pre- and postnatal hemodynamics in this congenital anomaly of the heart are discussed briefly.

I wish to thank Dr. E. W. Stizel, Dr. L. C. Burket, and Dr. Ch. I. Stoner for the permission to publish these two cases.

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Aneurysm of the Ascending Aorta Caused by Congenital Syphilis

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Congenital syphilis is an infrequent cause of aneurysm of the ascending aorta. Such a diagnosis is difficult to make since this aneurysm must be differentiated from that of acquired syphilis, rheumatic fever, congenital malformations, and various infections. Indentification depends on the presence of several factors, among which are family history of syphilis in parents and siblings, stigmata of congenital syphilis, positive serologic test for syphilis, early development of cardiac symptomatology and findings, and post-mortem confirmation of syphilis. Diagnosis is particularly difficult when rheumatic fever and congenital syphilis occur in the same individual. We wish to report a case of aneurysm of the ascending aorta which, clinically, is well established as being due to congenital syphilis.

CASE REPORT

A 20-year-old white man was admitted to Fitzsimons Army Hospital, in July, 1957, with a chief complaint of episodes of severe anterior chest pain. He felt well until 3 months previously when he experienced acute, severe epigastric pain which radiated to the anterior chest, into the neck, and down the left arm to the wrist. The pain was continuous, lasted 3 days, and was aggravated by deep breathing. Subsequently, he experienced three or four similar episodes but did not seek medical attention. The only other symptom was occasional shortness of breath on exertion. There was no history of rheumatic fever. A roentgenogram made at the time of routine physical examination revealed a mass in the mediastinum; this finding led to his transfer to this hospital.

Physical examination revealed a well-developed white man apparently in good health. Blood pressure was 110/50 mm. Hg in both arms, and the pulse was 96 per minute. The pupils were round, equal, and reacted to light and accommodation normally. Inactive interstitial keratitis was present bilaterally. The palatal arch was rather high, and "Hutchinson's teeth" were present. There was obvious pulsation of the chest wall in the first, second, and third intercostal spaces to the right of the sternum. A definite left ventricular lift was palpable at the apex, and a diastolic thrill was palpable at the base of the heart. Auscultation revealed the presence of a classical diastolic murmur of aortic insufficiency, best heard at Erb's point. The remainder of the physical examination was normal.

Roentgenograms of the chest (Figs. 1 and 2), roentgenkymograms, and fluoroscopy showed a large pulsating aneurysm of the ascending aorta, with calcification in its walls. Cardiolipin micro-

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flocculation test was positive without titer. The *Treponema pallidum* immobilization antibody test was invalidated on two occasions because of nonspecific Treponema immobilizing factors. The electrocardiogram and spinal fluid examinations were normal. Review of the patient's preinduction film made on May 21, 1956, revealed dilatation of the ascending aorta which had progressively enlarged over the ensuing months.

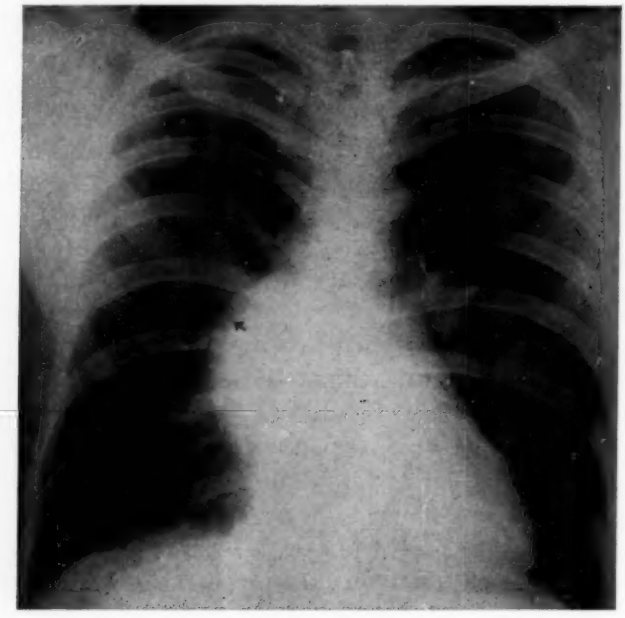

Fig. 1.—Posteroanterior roentgenogram of the chest, July, 1957.

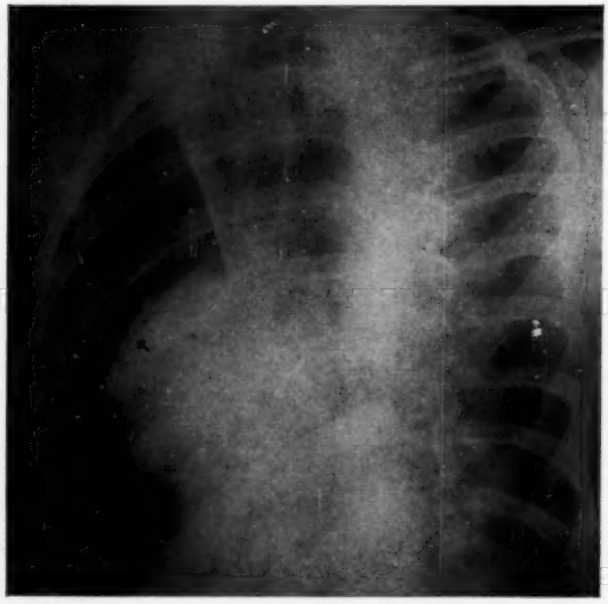

Fig. 2.—Left anterior oblique roentgenogram of the chest, July, 1957.

The following past history was verified by records of the West Virginia State Department of Health. The patient was born as an only child in 1938. In 1940, the patient and both parents were found to have syphilis. Each received therapy with arsenic and bismuth in 1940 and 1941, but the exact duration and amount of therapy are not known. In 1944, the patient received additional treatment for congenital syphilis, but type and quantity were not recorded. In 1951, the Mazzini test was positive and the Kahn test doubtful.

Palliative surgery for this patient's aneurysm was considered not feasible, and he was treated with 900,000 units of procaine penicillin every other day for ten injections and then discharged from the military service.

DISCUSSION

Clinically, this case fulfills the requirements for a diagnosis of aortic aneurysm caused by congenital syphilis and lacks only post-mortem confirmation. Even pathologic identification is absolute only if *Treponema pallida* are demonstrated in the aorta, and Stolkind[1] has emphasized that they are not found in the aortas of children with congenital syphilis who are more than 1 year of age.

Congenital syphilis may affect the cardiovascular system by producing variable lesions. These lesions have been most aptly classified by Hinrichsen[2] in her exhaustive review of the literature, as follows: (1) *Myocardial involvement.* This is a common pathologic finding in syphilitic stillborn infants, and in infants dying in the first few months of life. It has two forms, a diffuse interstitial myocarditis, and a focal nodular myocarditis. Each occurs with equal frequency and may cause sudden death in infants. Residual fibrotic scarring is not clinically recognized with certainty in older individuals. (2) *Aortitis in infants.* This lesion is identical histologically with the early aortitis of acquired syphilis. Infrequently, it gives rise to aortic aneurysms seen in older children and young adults. (3) *Aortitis and aneurysm in older children and adults.* Such a late manifestation of congenital syphilis must be differentiated from the aneurysm produced by rheumatic fever, congenital malformations, and various infections. Pathologically, it is identical to that of acquired syphilis. (4) *Congenital malformations of the heart occurring with congenital syphilis.* Reports of such conditions are rare and association apparently coincidental. (5) *Peripheral vascular lesions.* These consist primarily of an endarteritis, with or without aneurysm, producing local manifestations dependent on the severity of the vascular disease. They may be distributed widely throughout the body.

The frequency of involvement of the aorta in infants with congenital syphilis is unknown. Rach and Wiesner[3] reported involvement in 59 per cent of 27 cases studied. Similar incidence was reported previously by Bruhn.[4] Scharpff,[5] in a detailed study of serial sections of thoracic aorta, stated that the changes described by previous authors could be demonstrated in the normal fetal aorta. The problem is unsettled and further hampered by a disappearing source of material.

The diagnosis of aortitis in syphilitic infants is tenuous and can only be suspected. Beretervidi and Beretervidi[6] made this diagnosis if they could demonstrate fluoroscopically an aorta which was broader than normal for the child's age. Gesteira[7] based the diagnosis on the presence of an abnormally loud or tambour-like aortic second sound. Post-mortem confirmation was not included by either author.

The late development of aortic aneurysm from the aortitis of syphilitic infants must be very infrequent. In Hinrichsen's[2] review of the literature in 1943, there are reports of 25 cases which are supported by post-mortem examination, and reports of 26 cases which are based on clinical grounds alone. Subsequent reports have dealt with decreasing numbers of cases. McCollach[8] reviewed 498 cases of congenital syphilis over 2 years of age and found 5 cases with heart disease, all of which were rheumatic in origin. Givan[9] reviewed 417 cases of congenital syphilis ranging in age from 3 months to 42 years and found no instances of clinical heart disease. Laird[10] analyzed 115 cases of late congenital syphilis and made no mention of cardiovascular involvement. Various theories have been presented to explain the infrequent observation of disease of the heart and aorta due to congenital syphilis. It would seem logical that such cases may be missed because of a lack of data on serologic studies of the parents before and after birth of the child, leading to an erroneous later diagnosis of acquired syphilis. It also is more probable that early treatment of congenital syphilis may prevent the later development of cardiovascular disease.

SUMMARY

A case of aortic aneurysm probably caused by congenital syphilis is presented. Diagnosis is based on clinical grounds. Problems concerning identification and incidence are reviewed.

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Book Reviews

MOVEMENT OF THE HEART AND BLOOD IN ANIMALS, AN ANATOMICAL ESSAY. By William Harvey. Translated from the original Latin by Kenneth J. Franklin and now published for the Royal College of Physicians of London. Springfield, Ill., 1957, Charles C Thomas, 209 pages.

By far the best, this is the fourth translation into English since the anonymous one which appeared in 1653, during Harvey's lifetime, but regarding which we have no record of his opinion. The reasons for its excellence are not far to seek. Professor Franklin is not only an accomplished author but an expert both in physiology and—a rarity nowadays—in classical and Renaissance Latin, witness his masterly translations of Fabricius on the *Valves of the Veins* and of Lower's *De corde*. He does not try to write seventeenth century English nor, on the other hand, does he dodge difficulties by paraphrasing them in modern scientific terms that would bewilder Harvey more than the modern reader is puzzled by the obscurities of the old ideas or of the language in which they are expressed. He shows the advisability of retaining, in some passages, such topsy-turvy old terms as "vein-like artery" for pulmonary vein.

The Latin text occupies the last half of the book, which is a handsome production, printed in Oxford. It is to be hoped that Professor Franklin may yet be able to complete Harvey's writings on the circulation, by making a fresh translation of the two letters written to Riolan in 1647, nearly 20 years after the *De motu*, in the vain attempt to convince his old friend and chief opponent. "Search out the secrets of nature by way of experiment" was Harvey's admonition, and this golden work, the foundation of modern medicine, is still a model of the experimental method. Every student should be required to read it.

W. W. F.

PORTAL HYPERTENSION. By Allen Henderson Hunt, Baltimore, 1957, William & Wilkins Company. Price $8.50.

This contribution to the study of portal hypertension was the subject of the Jacksonian Prize essay of the Royal College of Surgeons of London, England, 1956.

The report is based on an analysis of 250 patients with portal hypertension seen personally by the author during the period 1947 to June, 1956. The patients were preselected and represented the more complicated cases which failed to respond to medical management and, hence, were referred for surgical opinion. Each case had been thoroughly assessed as to the etiology, clinical signs, and symptoms, and the data is here presented.

The anatomy of the hepatic circulation and the causes of portal obstruction are reviewed. Thirty-two cases were of the extrahepatic type, 19 were congenital, 13 of these being due to cavernomatous replacement of the portal vein. Splenoportograms of 5 of these patients are included in the text. Two hundred and eighteen cases of intrahepatic obstruction due to portal cirrhosis were noted—44 per cent were idiopathic, 45 per cent postinfectious, 12.4 per cent postalcoholic, 7.9 per cent biliary, and 6.9 per cent due to malnutrition.

A classical description of the effects of portal obstruction and the clinical signs and symptoms of cirrhosis and portal hypertension follows.

Several chapters are devoted to the problem of assessing the degree of portal hypertension. The portal pressures, portal venography, and the rate of portal blood flow were measured at operation with the abdomen opened. The rate of portal blood flow was determined by the use

of radioactive sodium. A normal portal blood flow was noted as being 8.7 cm. per second in controls and 4.4 cm. per second in patients with severe cirrhosis. The author notes that the role of portal hypertension was difficult to assess, in that, occasionally, bleeding varices may be present with normal portal venous pressures, or there may be an increased portal venous pressure without evidence of obstruction or varices. The author maintains that the portal venous pressure alone must not be used as an indication for operation, but that each individual case must be assessed in an effort to determine the etiology, because the therapy will vary with the underlying cause. Thus, intrahepatic obstruction was best treated by portacaval anastomosis, whereas extrahepatic obstruction and cavernomatous malformations responded, generally, in an unsatisfactory way to any shunting procedure. High portal pressures were observed to be due to external pressure on the portal vein by cysts or tumors. Removal of the local cause is the preferred treatment. Primary splenic disease was also noted to be associated with a high portal venous pressure, and in a large percentage of these cases splenectomy resulted in some improvement.

Portacaval anastomosis was shown to be the most valuable procedure for the control of hemorrhage, being successful in 87, 70, and 44 per cent, with a mortality of 0, 10, and 40 per cent in mild, moderate, and severe cirrhosis, respectively.

The book contains an extensive appendix which details the procedures used for measuring the portal venous pressures, portal venography, and the radioactive sodium test to determine the rate of portal blood flow.

A detailed description of surgical procedures for portacaval anastomosis, lienorenal shunt, transgastric and esophageal resection, and ligation of esophageal veins is included, while some points on the hazards and pitfalls of surgery in this region are noted which will be of prime interest to the surgeons. There is also a clinical note on 112 selective cases, and an extensive bibliography.

This is an excellent review of the subject of portal hypertension, with an orthodox presentation of the anatomy, physiopathology, and the medical and surgical management of these cases. It is well produced, with large, easily readable type, is profusely illustrated, and may be recommended for both the undergraduate and postgraduate student. The internist and the surgeon interested in the problem of liver disease and portal hypertension will find this monograph a useful record of an extensive clinical experience which shows what enthusiastic treatment and careful supervision can do for these patients.

A. A.

Announcements

THE ANNUAL MEETING OF THE AMERICAN SOCIETY FOR THE STUDY OF ARTERIOSCLEROSIS will be held in San Francisco, Calif., Oct. 22 to 26, 1958.

THE THIRD INTERNATIONAL CONGRESS OF ANGIOLOGY will be held in Sanremo, Italy, Sept. 24 to 28, 1958.

Letters for accommodations should be addressed to the Sanremo Travel Agency, Palazzo Riviero, Sanremo, Italy.